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THE ARGUMENT FOR CHEMICAL MEDIATION OF NERVE IMPULSES[1]

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WHEN an impulse travels along a nerve it is attended by a quick rise of negative electrical potential, followed by a quick fall. The duration of this "spike potential" includes the absolutely refractory and the relatively refractory periods of nerve function. The fall is not immediately to zero, but is checked by a slower, negative after-potential. And that in turn is followed by a longer, positive after-potential. The changes are more rapid in fibers of large diameter than in small fibers; the spike lasts only 0.4 msec. in the fastest fibers (*e.g.*, those supplying skeletal muscles) and thereupon the nerve can be stimulated again.[2] As elsewhere in the body, such electrical phenomena are signs of physicochemical or chemical processes which accompany functional activity. In nerve there must be to a large extent a restoration of the resting state, when an impulse has passed, before another impulse can traverse the same course. Associated with the electrical phenomena of nervous activity is a use of oxygen, an output of carbon dioxide and a display of heat. Since a nerve soon ceases to transmit impulses in the absence of oxygen, it is reasonable to assume that the increased metabolism, demonstrable when a nerve functions, indicates that chemical work is involved. According to evi-

[1] The annual Alpha Omega Alpha address, given on October 13, 1939, at the celebration of the fiftieth anniversary of the founding of the Medical School of the University of Minnesota.

[2] H. S. Gasser, Harvey Lectures (Baltimore), 32: 169–174, 1937.

dence furnished by Schmitt and Gasser,[3] the negative after-potential depends on active oxidation. It is depressed by asphyxia, and after asphyxia it is much augmented by conditions which favor oxidation. And when this potential is augmented the rate of recovery is hastened. It is highly probable, therefore, that even in the subsidence of the spike potential—for in fibers of fast conduction the negative wave "is first seen at its maximal value"[4]—an oxidative restorative process occurs, essential for returning to the nerve the ability to act again.

The electrical theory. The spike potential, sweeping along a nerve which has been effectively stimulated, causes an electric current to run, in a conductor external to the nerve, from inactive points to the active region, the "action current." It is assumed that a polarized state exists in the surface membrane of each nerve fiber (the outer charges positive); that a stimulus decreases or abolishes the potential difference across the membrane at a node of Ranvier, thus making it permeable and depolarizing it; and that thereupon adjacent nodes of the fiber discharge through the node already discharged so that new nodes in turn become permeable, depolarized and activated, and cause next proximal nodes to do the same. That the circulating local currents resulting from this traveling negative electrical wave can cause stimulation of successive portions of a nerve has been proved by Hodgkin,[5] who has demonstrated that, when an impulse reaches a region blocked by cold or compression, the local currents extend beyond the block and set up there a change of potential with an accompanying change of excitability. Blair and Erlanger[6] have brought supporting evidence by showing that an action current will pass an inert polarized region of the nerve and stimulate the responsive segment beyond. According to the traditional theory of transmission of influence from neurones to other neurones (as in a sympathetic ganglion) or from neurones to the cells of an effector organ (a muscle or gland), that is the sort of process which occurs—it is supposed that the local circuits reach beyond the limits of the active nerve and excite, electrically, the next element in the series.

At the synapse between neurones and effectors there is evidence of a protoplasmic discontinuity. As Bronk and Brink[7] and also Forbes[8] have pointed out, this introduces a physical condition not found in Hodgkin's experiments. As Forbes has remarked, "The structural and presumably the electrical conditions are quite different in an unbroken but inactive axon from those at the synapse. Here, at the termination of the neurone, histology seems to reveal a transverse membrane, which may well act as a short circuit to the action potential. . . . If the membrane theory of nerve conduction holds good, there is every reason to expect such a short-circuiting effect at the termination of the axon." Furthermore, Rosenblueth and I[9,10] have shown that smooth muscle—that of the nictitating membrane—though readily responsive to a single nerve volley, is, after being deprived of its nerves, quite unresponsive to a single electric shock. Similarly, the cells of a gland (the adrenal medulla in our tests), easily activated by impulses delivered by their nerve supply, are, after denervation, affected to only a very slight degree, even when electric shocks are applied so powerful and prolonged as to injure the tissue. Obviously, there are synapses at which the possibility of stimulation by the action current appears to be highly improbable.

The chemical theory. In recent years evidence has accumulated that when an impulse arrives at a nerve ending it sets free a chemical substance—adrenaline at sympathetic synapses, acetylcholine at parasympathetic synapses and at synapses in motor end plates and in sympathetic ganglia—and that these substances rouse in the next distal element its typical reaction—secretion, contraction, relaxation or nervous conduction. Two theories of synaptic transmission have been proposed—the traditional electrical theory and the newer chemical theory. Each theory has its ardent advocates, and a vigorous controversy prevails between them. For purposes of the present discussion these advocates may be called the "electragonists" and the "chemagonists"—"agonist" meaning contestant or combatant!

There is agreement of the agonists on certain points. In order to simplify the consideration of these points, and also the points of difference, I propose to limit the present discussion to synapses in which there is evidence that acetylcholine is involved. The liberation of this substance at parasympathetic synapses and at the synapses of sympathetic ganglia and motor end plates, on the arrival of nerve impulses, is frankly admitted by the electragonists. They also admit that tissues where acetylcholine appears contain a cholinesterase which quickly destroys that highly unstable combination of choline and acetic acid. They admit, further, that acetylcholine, when perfused in very minute amounts through organs in which it is dis-

[3] F. O. Schmitt and H. S. Gasser, *Am. Jour. Physiol.*, 104: 320, 1933.
[4] H. S. Gasser, *loc. cit.*
[5] A. L. Hodgkin, *Jour. Physiol.*, 90: 193, 211, 1937.
[6] E. A. Blair and J. Erlanger, *Am. Jour. Physiol.*, 126: 97, 1939.
[7] D. W. Bronk and F. Brink, *Ann. Rev. Physiol.*, 1: 398, 1939.
[8] A. Forbes, *Jour. Neurophysiol.*, 2: 465, 1939.
[9] A. Rosenblueth and W. B. Cannon, *Am. Jour. Physiol.*, 108: 384, 1934.
[10] W. B. Cannon and A. Rosenblueth, *Am. Jour. Physiol.*, 119: 221, 1937a; *C. r. Soc. de Biol.*, 124: 1262, 1937b.

arged by nerve impulses, will influence these organs do the impulses themselves. They admit, likewise, at when present in excess acetylcholine has not a imulating but a paralyzing action. And, finally, ey admit that the acetylcholine naturally set free at rasympathetic endings in slowly reacting structures *e.g.*, in the heart, smooth muscle and glands—is the ent which affects these structures. The main differ- ce now concerns the rôle of this mediator in the ansmission of influence from nerves to skeletal uscle cells and from nerves to nerve cells at gang- onic synapses. Electrical stimulation will, indeed, cite both muscle cells and nerve cells; and therefore e action current, if it reaches with effective intensity yond the junctions, would act as a stimulus. But, that is the mode of transmission, why the discharge acetylcholine by the nerve impulse? This is where eories begin to conflict.

In evaluating two antagonistic theories, nothing is be gained by a recital of the phenomena which both n explain. Deeper insight into the processes con- rned in the theories is likely to result from a survey the phenomena which only one, or neither, can count for. On that basis we may proceed to com- are the two theories—electrical and chemical—as xplanations of observed facts.

A comparison of the electrical and the chemical heories. First, the analogy between evidence for hemical mediation in the slowly responsive heart nd evidence for it in rapidly responsive striate muscle nd sympathetic ganglia. In all three structures a erfusate obtained while they are not stimulated con- ins no demonstrable acetylcholine. In all three, erve-stimulation causes the appearance of acetyl- holine, though eserine may have to be used to prevent s sudden destruction by cholinesterase. In all three, erfusion with acetylcholine induces the typical effects f nerve impulses—inhibition of the heart beat, con- raction of skeletal muscle and discharge of ganglion ells. And in all three the effect of acetylcholine can e blocked by drugs, without preventing its liberation t nerve endings—in the heart by atropine, in striate uscle by curare and in the ganglion by nicotine. Under these conditions, with nerve impulses delivered o the tips of the active nerve fibers, as shown by the ischarge of acetylcholine there, and with the re- ipient elements still sensitive to electrical stimula- ion, the action current is without influence.

The practical identity of evidence for chemical mediation in the three regions raises pertinent ques- ions. If the action current is the true transjunctional timulus, what is the use of acetylcholine, regularly produced during stimulation? How is the efficacy of minute amounts of acetylcholine, as a stimulus to ganglion cells and muscle fibers, to be accounted for? Why should there be a concentration of cholinesterase in sympathetic ganglia and at the motor end plate (*cf.* Marnay and Nachmansohn, 1937;[11] Feng and Ting, 1938?[12] The electragonists surely face difficulties in answering these questions, difficulties not encountered in the chemical explanation. The orthodox electragonists, moreover, are inconsistent; they agree that acetylcholine is a deputy of nerve impulses at vago-cardiac synapses, but deny it that function for neuromyal synapses. Furthermore, they confront a dilemma—on the one hand, agreement that acetylcholine is a chemical mediator of nerve impulses, and on the other, admission that the wide-spread arrangements for its routine production and prompt destruction at synapses, where it can stimulate, are merely a false and futile show. In attempted avoidance of this dilemma hypothetical suggestions of imaginary functions have been offered, *e.g.*, that acetylcholine may serve to increase excitability at synapses, or to delay the onset of fatigue, or to dilate blood vessels locally, or to exert vague "trophic influences."[13] Perhaps it "may"; but it can demonstrably do things to muscle cells and to sympathetic neurones; it can excite in them their peculiar functions. Confessedly, the argument implied in emphasizing the presence and capacity for action of acetylcholine at synapses is based on the reasonableness of means being adapted to ends. In biology, however, that argument is so generally valid as to be, in special cases, quite respectable.

The electragonists have set up what they regard as a serious obstacle to the chemical theory in stressing the brevity of the latent period of the postsynaptic elements before action occurs. In supporting this criticism Fulton[14] has expressed the judgment that "synaptic transmission is probably brought about directly by the action currents of the axon terminal rather than by a specific humoral agent such as acetylcholine," which, in his opinion, "appears to be a by-product of nerve metabolism." It is true that the synaptic events are very brief. In the neurones of the superior cervical ganglion the latent period of the most rapid responses ranges from 2 to 4 msec.,[15] and in the fibers of some skeletal muscles it can be shorter, 1 to 2 msec. (Eccles, footnote 13). If acetylcholine is the transmitter it must flash forth and excite in that brief time; and since a single nerve volley induces a single response the acetylcholine must be quickly rendered ineffective during the refractory phase of the responding elements (which lasts in neurones and muscle fibers about as long as the latent period) be-

[11] A. Marnay and D. Nachmansohn, *C. r. Soc. de Biol.*, 125: 41, 1937.

[12] T. P. Feng and Y. C. Ting, *Chinese Jour. Physiol.*, 13: 141, 1938.

[13] J. C. Eccles, *Physiol. Rev.*, 17: 538, 1937.

[14] J. F. Fulton, "Physiology of the Nervous System." New York, 1938.

[15] G. L. Brown, *Physiol. Rev.*, 17: 485, 1937.

fore another nerve volley can act again. The time is too short, the electragonists assert, for these chemical changes to occur. It is pertinent to point out that this is an assumption. Too little is known of the speed of chemical processes at synapses to justify categorical limitations. Furthermore, the electragonists neglect the fact that the nerve fiber itself, when it transmits an impulse, must recover before it can transmit another. Evidence indicates, as we have noted, that this recovery is an oxidative chemical process, and in fast mammalian fibers it lasts less than 1.0 msec., *i.e.*, it may be much more rapid than the transmission at ganglionic and muscular synapses, which the electragonists assume to be too rapid to be chemical. Until they can offer better evidence for their assumption they have a frail basis for belittling the speed of intimate molecular changes.

The argument that the delay at synapses is too short for the processes required by the chemical theory can be turned against the electragonists. When an electric current is applied to a nerve, the interval between the instant of shock and the discharge of the nerve impulses ranges between 0.2 and 0.4 msec. The delay between the arrival of the impulse at the superior cervical sympathetic ganglion and the discharge of the ganglion cells is at least 5 times as long as that for the quickest cells and at least 11 times as long for the next quickest.[16] If a weak electric current can activate the nerve fibers almost instantly, and the electric action current activates the ganglionic neurones, as the electragonists argue, why this protracted latent period? The relatively long delay in the ganglion is matched by a similar delay in the motor end plate. Here the electragonists have a real problem. The chemagonists, on the other hand, can readily account for the extra time as due to the requirements of an interposed chemical mediation.

At this point may be mentioned an attempt to bring electrical events in the ganglion into relation to electrical events in the nerve trunk. As shown by Gasser and Erlanger[17] and Graham and Gasser,[18] nerves have a heightened electrical excitability during the negative after-potential and a decreased excitability during the subsequent positive after-potential. These two phases, negative and positive, following the spike potential, can also be recorded from the ganglion after it has been stimulated; and Eccles[19] has claimed that submaximal volleys of nerve impulses delivered to the ganglion during its negative after-potential evoke smaller spikes than the original. These observations, if confirmed, might bring support to the electrical theory. In the present discussion a detailed review of the evidence and arguments against Eccles's contentions is impossible. Suffice it to remark that Rosenblueth and Simeone[20] have recorded variations of the spike potentials of the ganglion, responding to maximal and submaximal stimulation, that were precisely opposite to what the inferences of Eccles would predict—maximal spikes when the ganglion was maximally positive, and noteworthy decrease of the spike at the peak of the negative phase. Furthermore, they noted that by altering conditions the synaptic delay could be shortened to less than 1 msec. or increased to twice its usual length. Because of the lack of correlation between after-potentials and the responsiveness of the ganglion cells and also because of the large variations in synaptic delay, as well as for other reasons, Rosenblueth and Simeone concluded that the electrical theory, instead of being in agreement with observed facts, is definitely opposed by them.

Evidence for the chemical theory from experiments with curare. The action of curare confronts the electragonists with a perplexing question. As is well known, this drug is capable of paralyzing muscles by interrupting the nervous influence at the neuromuscular junctions. It does not, however, prevent the discharge of acetylcholine at the nerve endings; the nervous action currents, therefore, run their full course. And with small doses of curare the inherent irritability of the paralyzed muscle is not altered.[21] Yet the muscle does not respond to the nerve impulse. The paralyzing effect of curare at the motor end plate offers no difficulty for the chemical theory. What curare does is to reduce the sensitiveness of the responsive element in the plate. In studies on denervated skeletal muscle Rosenblueth and Luco[22] demonstrated that even with doses too small to stop action of the respiratory muscles curare markedly lessens the contractions resulting from uniform injections of acetylcholine. And the same phenomenon is seen in normally innervated skeletal muscle.[23] In short, curare acts as if it raised the threshold to acetylcholine. Then the normal amount of the mediator which is released by the nerve impulse is incapable of causing the muscle to contract. Thus, while a curare paralysis displays a phenomenon hard for the electragonists to explain, it forms a part of the factual support for chemical transmission.

[16] J. C. Eccles, *Jour. Physiol.*, 85: 179, 1935.

[17] H. S. Gasser and J. Erlanger, *Am. Jour. Physiol.*, 94: 247, 1930.

[18] H. T. Graham and H. S. Gasser, *Proc. Soc. Exp. Biol. Med.*, 32: 553, 1934.

[19] J. C. Eccles, *Jour. Physiol.*, 85: 464, 1935; 88: 1, 1936.

[20] A. Rosenblueth and F. A. Simeone, *Am. Jour. Physiol.*, 122: 688, 1938.

[21] H. Grundfest, *Jour. Physiol.*, 76: 95, 1932.

[22] A. Rosenblueth and J. V. Luco, *Am. Jour. Physiol.*, 120: 781, 1937.

[23] G. L. Brown, H. H. Dale and W. Feldberg, *Jour. Physiol.*, 87: 394, 1936.

Recent studies on curarized end plates present the electragonists another hard problem to solve. In experiments performed by Luco and Rosenblueth[24] two symmetrical muscles (*e.g.*, the soleus of each side) were arranged to record simultaneously. After a paralyzing dose of curare had been injected the motor nerve of one of the muscles was stimulated continuously at the rate of 60 shocks per sec. When the control muscle was periodically tested through its nerve, and by its response proved that complete recovery from curarization had occurred, the continuously stimulated muscle was usually not contracting at all. If given a brief rest and then again subjected to the stimulation, it contracted momentarily and thereupon promptly became inert; *i.e.*, it manifested extreme fatigue. Clearly, this was not a fatigue of the muscle, for the curare throughout the whole period of stimulation had protected the muscle from being forced into activity. And it was not a fatigue of the nerve, for that remarkable structure can carry impulses at the rate of 60 per sec. during an indefinitely long time. Furthermore, records of the spike potentials proved that the nerve impulses might be full-sized when they were having no effect. The fatigue occurred at the point of transmission. Even if curare should somehow block the nerve action current, the electragonists would have trouble solving this riddle, because the curare block disappeared while the continuous stimulation of the nerve was evoking no muscular contraction. In other words, at a time when both the electrical excitability of the muscle and the spike potentials of the nerve were quite normal, the nerve impulses failed to stimulate. Before this situation the electrical theory breaks down. The chemical theory, on the other hand, has no trouble in explaining it. Prolonged rapid stimulation results, after an initial large outburst of acetylcholine, in a gradually reduced discharge until the concentration falls below the effective range.[25] In these circumstances, according to the chemical theory, a muscular response would not occur. And it does not.

Evidence from experiments with eserine. In order to introduce another important series of facts supporting the theory of chemical transmission at muscular and ganglionic synapses, I wish to present evidence regarding the action of eserine. (That term will be used as equivalent to physostigmine and prostigmin). It will be recalled that eserine is able to protect acetylcholine against destruction by a cholinesterase. It will be recalled, also, that if acetylcholine is present in excess it is not a stimulating agent but a depressant.

As Rosenblueth and Morison[26] demonstrated, eserine has quite opposite effects on two symmetrical muscles, one recording responses to slowly repeated nerve impulses, the other responding to similar but rapid stimulation. A small intravenous injection of eserine causes the less frequently stimulated muscle to contract more strongly, and simultaneously it causes the corresponding, more frequently stimulated muscle to contract less strongly. This very striking difference of effect is not due to altered action currents, for the intensity of the nerve spike potential is not affected by eserine. Eccles (*Ergebn. d. Physiol.*, 38: 339, 1936) has suggested that eserine exerts its influence by increasing the sensitiveness of the responding structures. Obviously that suggestion does not apply to the depressant effect on the rapidly stimulated muscle. That effect has its explanation in the change produced in the functioning of such a muscle when acetylcholine is injected so that it is present in excess; the contractions are depressed as they are depressed by eserine. The action of eserine, therefore, can reasonably be accounted for, in these circumstances, by its shielding of the acetylcholine as it is set free by the nerve impulses, against attack by cholinesterase. Since the impulses are quickly recurring, the time for destruction is abbreviated, and with protective eserine at hand, the acetylcholine accumulates until it reaches a concentration which paralyzes some of the end plates. Thus would the chemagonists clear up the phenomenon.

But how account for the opposite effect in the slowly stimulated muscle? That, again, finds an explanation in the shielding of acetylcholine by eserine. Under normal conditions a single volley of nerve impulses evokes a single response in a muscle, as registered by the spike potential of the muscle fibers. If eserine is administered, however, a single volley from the nerve induces a repetitive response and hence a greater muscular shortening. As Brown, Dale and Feldberg[27] have pointed out, this sort of response to single volleys after eserine may reasonably be attributed to the persistence of the acetylcholine released by the motor impulse at the neuromuscular junctions.

The only difficulty which the chemagonists meet in clarifying the remarkably opposed effects of eserine on slowly and on rapidly stimulated muscles is that of understanding why these effects are prolonged. It is known that potassium ions are liberated simultaneously with acetylcholine, and they, as persistent agents, may play a rôle not yet evident. Whatever may be the final chapter of this story it is clear now that the results of injecting eserine are such as to

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[24] J. V. Luco and A. Rosenblueth, *Am. Jour. Physiol.*, 126: 58, 1939.

[25] G. L. Brown and W. Feldberg, *Jour. Physiol.*, 88: 265, 1936.

[26] A. Rosenblueth and R. S. Morison, *Am. Jour. Physiol.*, 119: 236, 1937.

[27] *Loc. cit.*

place still unsurmounted obstacles in the path of the electragonists, while presenting the chemagonists additional support for their views.

Evidence for the chemical theory from experiments with different rates and periods of stimulation. Thus far the discussion has been concerned mainly with transmission at neuromuscular synapses. Many years ago Elliott[28] called attention to striking resemblances between characteristics of motor end plates and of cell bodies in sympathetic ganglia. For example, nicotine in small doses stimulates at both places, and in larger doses it paralyzes both; curare blocks transmission to skeletal muscle, and in greater concentration it has a similar influence in the ganglion; and, whereas the postganglionic axons can not replace motor fibers, the preganglionic axons, effective on the ganglionic cells, can be cross-sutured and will grow out and make good functional union with striated muscle cells. To these resemblances we can now add the following: acetylcholine in small doses excites at both synapses; and when present in excess acetylcholine, like nicotine, has a depressant or paralyzing influence. We have learned recently that there are still other remarkable similarities between these two transmission points. It will be convenient, therefore, to consider them together.

As shown by Rosenblueth and Morison,[29] if a muscle is stimulated through its nerve at a rapid rate—*e.g.*, 240 shocks per sec.—the muscle first shortens in a sharp strong contraction, then changes promptly to a low contraction or fails to contract at all, and thereupon it shortens in a strong contraction again. Thus with recurring impulses of a constant high frequency the muscular response manifests three distinct stages—a sequence of plus, minus, plus. Now if the stimulation is continued the muscle enters a well-known fourth stage, that of lessened efficiency or fatigue. If the stimulation is at a slow rate from the start, stages 2 and 3 drop out; then stage 1 merges directly with stage 4. Curiously enough, as revealed in the experiments of Rosenblueth and Luco,[30] continuance of the stimulation at a slow fatiguing rate (60 per sec.) causes the muscle to enter gradually a fifth stage in which its performance progressively improves; the contractions increase in strength—displaying a tension as great as 60 per cent. of the highest tension developed at the beginning—and this betterment may last for several hours.

By use of the nictitating membrane of the cat as an indicator of the discharge from the superior cervical sympathetic ganglion the effect of stimulation of preganglionic fibers on the ganglion cells can be examined. In experiments which Rosenblueth and I[31] performed we were able to duplicate, with rapidly repeated stimuli, the first four stages—plus, minus, plus, minus—seen in skeletal muscle. The only difference was a preliminary dose of eserine in experiments on the ganglion. And a few months ago Lanari[32] and Rosenblueth succeeded in recording in the ganglion performance the fifth stage, that of partial recovery of the original efficiency, if only the fatiguing stimulation is patiently continued.

Here is a challenging sequence of events. Why do muscle cells and ganglion cells, when continuously stimulated, respond well at first, then poorly; well again, then poorly again; and finally well for a long period? As proved by Rosenblueth and Luco,[33] who took records of the nerve action potentials periodically during four or five hours of stimulation, there may be a slow diminution in the height of the spikes or there may be no diminution, but in no case is there any correlation between the electrical phenomena of the nerve and the various stages of muscular activity. These conditions at motor end plates and at ganglionic synapses—and with normal blood supply, let it be noted—disclose a puzzle which the philosophy of the electragonists has not dreamed of. What clue to its solution can the chemagonists present?

As previously remarked, when a nerve is continuously stimulated there is at first a flush discharge of acetylcholine at the nerve endings, and then the discharge gradually diminishes. Now if the stimuli are repeated at very high frequency time will be lacking for destruction of the relatively abundant acetylcholine by cholinesterase; thereby the initial great outburst becomes accentuated and the acetylcholine accumulates until it is present in a paralyzing concentration. Thus, the primary contraction of the muscle (stage 1) is quickly followed by less contraction or an actual failure to contract (stage 2). In the ganglion a small dose of eserine, protective against the destructive cholinesterase, allows the acetylcholine to act in the same manner, so that it has the same paralyzing effect. As the primary outburst quickly subsides, the depressant concentration of acetylcholine ebbs away, to be replaced by an optimal lower concentration which is highly stimulative; hence the rise of the muscular tension into stage 3. That this is the correct explanation is proved by the injection of a small amount of acetylcholine during stage 2, whereupon the depressed condition is prolonged; or during stages 1 or 3, whereupon, not stimulation, but, instead, depression is induced. The fourth stage, the stage of fatigue, can be explained by so great a reduction in the output of

[28] T. R. Elliott, *Jour. Physiol.*, 35: 367, 1907.
[29] *Loc. cit.*
[30] *Loc. cit.*
[31] See footnote 10.
[32] A. Lanari and A. Rosenblueth, *Am. Jour. Physiol.*, 127: 347, 1939.
[33] *Loc. cit.*

acetylcholine that it fails to stimulate some of the cells; hence the lessened degree of response—*i.e.*, the appearance of "fatigue." That this interpretation is correct is proved by injecting at this stage the same dose of acetylcholine as that which caused depression in stages 1 and 3 and finding that it now causes an improvement of the response. This, of course, is strictly in accord with the theory of chemical transmission.

The astonishing recovery of function in the fifth stage has been investigated by Rosenblueth, Lissák and Lanari.[34] They have assayed the acetylcholine content of nerves, quickly frozen *in situ* by carbon-dioxide snow, or instantly excised and dropped into liquid air (in order to prevent any change), after continuous, rapid stimulation for various lengths of time. They found a progressive decrease in the content during the first ten minutes—a decrease which turned to an increase when there was a brief period of rest. In the fifth stage the concentration of acetylcholine had gradually increased over that in the fourth stage. If, now, it is assumed that depolarization of the surface membrane of the nerve fibers is attended by a greater permeability for the acetylcholine contained within them, the output per impulse would vary directly with the concentration. In the fifth stage, when the fibers have more acetylcholine, they give forth more, and the result is a larger response. This is the view presented by Rosenblueth, Lissák and Lanari. It is substantially based on the agreement between the evidence of acetylcholine liberation from nerves at the different stages of stimulation and the evidence of concentration of acetylcholine in nerve fibers.

I have described a group of events in the transmission of nerve impulses from neurone to neurone and from neurone to muscle cell. I can find no adequate explanation for these perplexing events in terms of the electrical theory. On the contrary, I can see that supporters of the theory of chemical transmission need only use demonstrated facts in order to give a reasonable answer to the whole intricate riddle.

Evidence for the chemical theory from degenerating nerves and muscles. The main assumption in the foregoing account of the five stages of transmission at peripheral synapses was that the output of acetylcholine per nerve impulse would vary with its concentration in the nerve fiber. The recent research by Rosenblueth, Lissák and Lanari, *loc. cit.*,[34] already noted, has furnished evidence that when a nerve has been cut and is undergoing degeneration there is a gradual reduction of the acetylcholine content after the first twenty-four hours. A highly significant fact is that during these first twenty-four hours no functional change is observable. As the concentration of acetylcholine diminishes in the second twenty-four hours, however, the possibility of evoking stage 5 is regularly lost, and stages 2 and 3 may largely disappear or be wholly absent. *At the same time the nerve spike potentials are of normal intensity.* The results are quite in accord with the assumption mentioned above, for, as will be recalled, tests revealed that stages 2 and 3 were due to an excess of acetylcholine and stage 5 to an improved production of it. In the degenerative process, with the acetylcholine of the nerve gradually becoming less, these periods of excessive production fade out and as they do so the attendant variations of activity likewise fade out. And, as might have been anticipated, the fourth stage, that of fatigue, becomes unduly emphasized—the transmission from degenerating nerves "fatigues" much sooner than normally. Now the further important fact emerges that while nerves in the late steps of degeneration can still conduct, as revealed by a definite, though reduced, spike potential, they may not stimulate across the synapse. All these observations harmonize perfectly with the chemical theory of transmission and find no illumination whatever in the electrical theory.

Perhaps no further testimony is needed to justify the claims of the chemagonists. There is one other observation, however, which is demonstrative and well worth presenting. As is now generally recognized, autonomic nerves do not end on striated muscle. They do end on blood vessels—vessels intimately distributed throughout striated muscle fibers. Among the autonomic nerves which give off acetylcholine is the lingual, supplied to the vessels of the tongue. In 1937 Rosenblueth and Luco recorded the action potentials of the tongue muscles which had been deprived of motor nerves for about a week. Stimulation of the lingual nerve induced the appearance of typical action currents in the completely denervated muscle fibers. Here is a stimulation of muscular units clearly not due to electrical transmission, for the nerve stimulated was not distributed to the muscle which responded, and, furthermore, the latent period (60 msec.) was too long for that occurrence. It was a clear instance of a contractile response to acetylcholine, liberated by nerve impulses, to be sure, but not nerve impulses delivered to the contracting fibers. Electrical transmission was definitely excluded. Until the electragonists can display an instance of electrical transmission without acetylcholine at neuromuscular and neuroneuronal synapses their argument can not be on the same footing as that of the chemagonists.

Meanwhile they have arduous tasks in explaining away the evidence which has repeatedly proved the adequacy of the chemical theory of nervous transmission.

[34] A. Rosenblueth, K. Lissák and A. Lanari, *Am. Jour. Physiol.* In press.

THE BASIC NEEDS OF AMERICAN ARCHEOLOGY

By Dr. CARL E. GUTHE

CHAIRMAN OF THE DIVISION OF SOCIAL SCIENCES, NATIONAL RESEARCH COUNCIL

LATE in April of this year there was appointed in the Division of Anthropology and Psychology of the National Research Council a committee to study the basic needs of American archeology. This committee is composed of W. D. Strong, *chairman,* Clark Wissler, A. V. Kidder, Fay-Cooper Cole, W. C. McKern, J. O. Brew and W. S. Webb. Before undertaking a detailed examination of the archeological problems, the committee felt that it was best to limit its sphere of interests by an analysis of the principles which govern the methods and procedures of American archeological research. At a meeting late in June a preliminary statement of these principles was prepared, upon which this article is based. This first report of the committee constitutes a declaration of the field of interest of the committee and indicates the nature of the basic needs of American archeology which will be studied in its future deliberations. Mimeographed copies of this preliminary report may be obtained from the Division of Anthropology and Psychology, National Research Council, 2101 Constitution Avenue, Washington, D. C.

The aim of American archeology is "to make the past live again," to preserve for posterity the story of the rise and spread of early cultures on this continent and their influence on white settlement. From such studies much can be learned, not only in the field of human history, but also of such significant subjects as long-continued land utilization, cycles of climatic change and the history of important agricultural crops. It is obvious that the competent archeologist must be completely trained in all aspects of anthropology and historical method, in order to be able to interpret these data adequately.

In every part of this country a great deal of excavation and collecting has been carried on, often by untrained persons and without well-defined aims. These activities have irrevocably destroyed many pages of unwritten American history.

More recently state and federal projects have been inaugurated, in some cases to afford employment, in others to rescue prehistoric records in districts about to be flooded. Out of these latter efforts, and through excavations carried on by universities and other scientific organizations, much experience and knowledge have been gained. These projects are being continued, and others are contemplated. It therefore seems urgent that this committee of the National Research Council set forth in brief form what it believes to be the minimum requirements for any future work, whether under public or private auspices.

In initiating an archeological research project, a definite need should be shown for the solution of a well-defined archeological problem or for the conservation of prehistoric material placed in jeopardy by public works or other agencies, whether natural or human. The program of the work should propose a comprehensive archeological investigation. The sponsoring scientific institution or learned society should be able to guarantee adequate supervision and field management, laboratory restoration and study of material, permanent conservation of all materials and records and the publication of a final report. The committee suggests it is essential in the case of all archeological projects sponsored by federal funds that the representative of the sponsoring agent should be approved by the Smithsonian Institution, whose national character and scientific attainments make it the most satisfactory qualifying agent in the country.

Field operations should be conducted by trained field men with academic training as well as field experience. The general supervision of the field work should insure that adequate records be kept and that the work be done with a clear comprehension of the problem under attack. Naturally a balanced supply of surveying instruments, cameras, tools, supplies and storage and transportation facilities must be available. The supervisory staff must be given time for experimentation, rechecking of records and data, and careful completion of operations begun, as well as for the preparation of a full and complete field report. Time limitations should never be permitted to induce rush tactics which might promote carelessness or curtail efficiency.

The laboratory phase of the project should be conducted by trained laboratory technicians and a sufficiently large staff to care for field material as rapidly as it is acquired. The general supervision of the work should insure close cooperation between laboratory and field work in order that each may aid the other in the solution of the problem. As many allied sciences as may be necessary should be brought to bear upon the laboratory investigation.

The methods and techniques used in an archeological project are different, of course, in the field and in the laboratory. Both phases of the project should be under the general direction of a director. The active field director should possess a comparative knowledge of methods of work and the ability to adjust or revise these to suit the particular conditions under which he is working. In organizing a field party, specific types of work should be placed in the hands of capable men under the immediate direction of competent super-

visors. In order to secure most efficient service on the part of all concerned, it is essential that responsibility be vested with corresponding authority.

In survey work the preparation of maps and charts is one of the primary objectives. An accurate map should show the relationship of a site to the natural and significant cultural environment. The more detailed working plan, whether based upon the grid system or other arrangements of reference points and lines, should insure accuracy both for the initial surface charts and for the vertical and horizontal records. In so far as possible the site nomenclature should be in accordance with a statewide plan.

The methods employed in excavation should be selected to facilitate the clearest perception of the archeological phenomena. The soil may be removed by peeling, by vertical sectioning, by horizontal stripping in arbitrary levels or by combining these several procedures as dictated by the specific nature of the problems involved and the peculiarities of the site. In all cases, work must be conducted in a manner which promises to disclose all available evidence on formation and structure, and to preserve all data on stratigraphy, age, time succession, cultural and historical activities and cultural processes.

In all field work, whether it be a survey or an excavation, complete documentation is essential. The progress of the work must be fully documented by charts and texts. There must be full recording of finds and associations, preferably by filling out a standard form to insure complete and comparable information. Finally, there must be well-organized and integrated identifications, including good and complete photographic records.

The satisfactory application of laboratory methods presupposes the existence of a well-equipped laboratory for the storage of materials and for their analysis in order to facilitate definition of types, cultural synthesis and broad cultural comparisons.

The many and varied activities of the laboratory consist of: the recording, preservation and technical analysis and study of all tangible materials, including physical anthropological data; the integration and filing of all documentary records; the coordination of material data with other data to determine culture complexes and relationships, as well as the origin and development of these cultures; and finally, the preparation of the manuscript report for publication.

All the foregoing activities are nullified unless followed by prompt publication. There are several essential steps in the realization of this final scientific objective. Firstly, the daily notes on excavations, plans of trenches, lists of finds and photographs should be typed and otherwise recorded from day to day. This is so essential that the appropriation for each project should provide for the necessary clerical assistance in the field.

Secondly, when the record is approved by the archeologist in charge, three complete copies should be made. Where projects are under government auspices, one of these should be deposited in the Smithsonian Institution. If the sponsoring institution possesses an adequate library, the second copy should remain there; otherwise, it should be placed in the library of the state university. The third may be used as the working copy of the archeologist in charge, but ultimately should be deposited in some important library.

Thirdly, adequate arrangements should be made to supply the archeologist in charge with time and clerical and technical assistance for the preparation of an adequate final report of the work. It must be remembered, in this connection, that the study of materials and the preparation of a final report normally requires at least as much time as is devoted to field work.

A satisfactory final report should contain at a minimum a statement of the problem attacked, a description of the methods employed, an adequate descriptive and illustrative review of the data and a final section containing such interpretations and conclusions as are justified by the data.

Finally, in establishing any archeological program, whether for purely scientific purposes or in conjunction with problems of state or federal employment, the basic need for national conservation must be given primary consideration. Not only should each site opened be excavated with the greatest care, the material completely studied, and the results fully published, but also certain sites in every area should be carefully preserved for research in the future as new techniques are developed. The fencing, restoration, marking and guarding of important prehistoric sites is particularly applicable at the present time, permitting as it does the use of local labor and the advancement of historical interest.

Such forward-looking activities should extend from the National Park Service on the one hand to State Historical Societies and municipalities on the other. They will advance the growth of national consciousness as well as scientific progress, and should receive every encouragement.

It should always be remembered that the number of archeological sites in the United States is strictly limited, and that once a site has been carelessly excavated its value is totally destroyed. These ancient ruins are really material documents that comprise the very stuff of American history. From them we may learn not only the manner in which the New World was originally settled and how its strongly individualized and truly remarkable civilizations arose, but also determine

the history and nature of various important American agricultural crops. In addition, the practical problem of the sequence and duration of postulated post-glacial climatic cycles may only be solved when the archeological record is clear.

For these and similar reasons, it is the fundamental belief of the Committee on Basic Needs in American Archeology of the National Research Council that unless the foregoing minimum requirements of scientific archeology can be fully met by any federal, state or local institution, it should not undertake archeological research.

OBITUARY

FLOYD KARKER RICHTMYER

ON November 7 death came without warning to Dean Richtmyer of Cornell University. He collapsed while preparing to go to a concert with his family, and before the doctor arrived he was dead from coronary thrombosis. Thus was struck down, in the full tide of amazing activity, a prominent figure of the Cornell campus and one of the most influential members of several learned societies and institutions.

Floyd Karker Richtmyer was born on October 12, 1881, in the rural community of Cobleskill, New York. He showed an early interest in scientific research as an undergraduate at Cornell University. After graduation in 1904 he married and taught for two years at Drexel Institute, Philadelphia; then he returned to Cornell as instructor in physics, and in 1910 was awarded the degree of Ph.D.

In his activities as a graduate student, the main lines and characteristics of Richtmyer's life work are already visible. Stimulated by E. L. Nichols to an interest in photometry, he presented a paper before the Illuminating Engineering Society in which he advocated more instruction in the subject of illumination for engineers and described a new laboratory course in the subject. Thus he showed an early interest both in educational problems and in the applied side of physics. For the subject of his Ph.D. research, however, he chose the photoelectric properties of the alkali metals. In this investigation he did the careful, clean-cut experimental work for which he possessed an unusual talent; and he also revealed his outstanding characteristics of looking at a set of data from all angles and extracting from them every possible conclusion. He was preeminently a man with a passion for doing things well; and he saw many things to do.

From this point, Richtmyer's career falls naturally into three periods. During the first, he taught physics for students of engineering and pursued his interests in applied optics. In the Illuminating Engineering Society we find him on the council and on several committees, acting as chairman of a committee on education. Furthermore, in 1916 he assisted in the organization of the Optical Society of America, and throughout his life he contributed greatly to the work of that society; he was president in 1920, and for 22 years he participated in the conduct of the *Journal*, becoming editor in 1933.

About 1918, however, when he became full professor of physics, Richtmyer began to turn toward other fields. After a brief interlude in the study of thin films he developed an interest in x-rays which was destined to be permanent and to establish him as an authority in the field. After spending a sabbatic year as "investigator" in the laboratories of the General Electric Company, he undertook at Cornell a series of well-planned and precisely executed measurements on topics related to x-ray absorption, the principal result of which was to establish the law that absorption due to ionization in a given shell in an atom is proportional to the cube of the wave-length of the x-rays and to the fourth power of the atomic number. Then, in 1927, as a result of several months in Siegbahn's laboratory in Uppsala, Sweden, he became interested in the faint x-ray lines known as "satellites." He proposed a new theory concerning the origin of these lines, ascribing them to jumps made simultaneously by two electrons in an ionized atom; and he made a series of experimental studies in an endeavor to support the theory. Later he himself recognized, in the light of further developments, that most of the observed satellites are probably due to a mechanism proposed earlier by others, namely, to a one-electron jump in a doubly ionized atom; but it is still possible that some of the faintest lines are of his double-jump type.

Richtmyer's interest in x-ray research continued to the end. He inspired and supervised a number of investigations which did much to clear up the subject of x-ray line widths and shapes; after 1930, however, the actual work was done by others. His enthusiasm and obvious mastery of fact and technique attracted many graduate students into his field, and during many years he had the help of an assistant. His attainments as a scientist were given recognition by his election as president of the American Physical Society in 1936, and as vice-president in charge of section B of the American Association for the Advancement of Science in 1930; and in 1932 he was elected to the National Academy of Sciences (councilor in 1938).

About 1931 began the third period of Richtmyer's activities, during which most of his time was devoted to administrative work of wide variety. In that year he became dean of the graduate school at Cornell. In this capacity he strove, with tact and infinite patience, for the maintenance of high standards, hampered by

the circumstance that he had neither a budget nor direct control over students' work. In 1931, also, he participated in the organization of the American Institute of Physics, and thereafter he contributed greatly to its management, as a member of the executive committee of the governing board and of several other committees. Finally, in the same year he participated in the founding of the American Association of Physics Teachers, of which he remained a member of the executive committee and served several years as vice-president (1935, 1936), president (1937, 1938) or associate editor of the *Journal*.

In spite of these new responsibilities he continued to be active in the American Association of University Professors, of which he was vice-president in 1932 and 1933; serving on various committees, he took the leading part as chairman of a committee which studied the effects of the depression on higher education. As dean of the graduate school he was also brought actively into the work of the Association of American Universities; besides membership on several committees, he acted as chairman of one on foreign student problems which did a great deal to improve the lot of foreign students in America. In 1938 he was chosen to be the first personal permanent secretary of the association. And, finally, he continued until 1937 to share in the work of the National Research Council, of which he became a member in 1923; he was chairman of the division of physical sciences from 1930 to 1935 and on the fellowship board from 1930 to 1937.

During later years Richtmyer's teaching was restricted to an occasional graduate course and a senior course of his own devising. The subject-matter of the latter he published in 1928 as a book, "Introduction to Modern Physics," in which he surveyed from the experimental standpoint the advances of the present century. In this book, as on the lecture platform, he showed himself a master of clear and forceful exposition. He was often invited to lecture on scientific or educational topics; during the last two years he gave at least 15 lectures on his experiences as a physicist accompanying the National Geographic Society-U. S. Navy expedition to the South Pacific to observe the solar eclipse of 1937.

Richtmyer was a member of many scientific societies. In Sigma Xi he headed a committee on revision of the constitution, and from 1924 to 1926 he was president. He also took a warm interest in the Cosmopolitan Club of Ithaca, doing a great deal to establish this club on a sound basis. He seemed to feel surest that here he had, beyond all possibility of dispute, accomplished something to benefit mankind. It was characteristic of him in general that he was always willing to lend a helping hand to others; there are many, within the university and without, who feel a deep personal sense of gratitude toward him for such assistance. This trait and his graciousness as friend and host won him many friends, both on and off the campus. His closest friends speak of his frankness, sincerity and modesty. His going leaves many with a sense of irreparable loss.

He is survived by his widow, Bernice Davis Richtmyer, and three children: Robert D., now instructor in physics at Stanford University, Sarah (Mrs. Mann) and Lawson E.

EARLE H. KENNARD

CORNELL UNIVERSITY

WILLIAM HENRY BROWN

WHEN an active and productive man, experienced and successful in research, in teaching, in the preparation of important texts and in administration, altogether too rare an association of talents, suddenly and unexpectedly dies at the relatively young age of fifty-five years, not only his colleagues and associates keenly feel his loss but science itself suffers. This statement applies preeminently to Dr. William Henry Brown of the department of botany, Johns Hopkins University, whose death occurred in Baltimore on the morning of November 9, 1939.

Dr. Brown's active and productive career centered in the Philippines, for with the exception of one short vacation trip to the United States in 1925, he resided there continuously for twenty-seven years, a very long term of tropical service. Yet his investigations and his publications have given him a distinctly wide and favorable clientele not only in the Philippines and in the United States, but in all parts of the world where botany is an established and recognized field of instruction and research.

Dr. Brown was born in Richmond, Va., on October 6, 1884, receiving his bachelor's degree from Richmond College in 1906. In the fall of 1906 he entered Johns Hopkins University, taking advanced work in botany under the late Dr. Duncan S. Johnson. In 1909, after Dr. Burton E. Livingston joined the Johns Hopkins staff, he became more and more interested in plant physiology, and in this year accompanied the latter as research assistant to the Desert Laboratory of the Carnegie Institution, Tucson, Ariz. As an interim appointment he also served as scientific assistant in 1908 at the United States Fisheries Laboratory at Beaufort, N. C. While a graduate student at Johns Hopkins University he served as graduate assistant in botany, was appointed a fellow in 1909, and, after receiving his Ph.D. degree in 1910, was appointed a Bruce fellow, a post-Ph.D. fellowship for studies planned to be carried on at the Desert Laboratory. In the fall of that year, however, he resigned the Bruce fellowship to accept an instructorship in plant physiology at Michigan State College. These brief data suffice to cover his formative years, but in whatever field he worked, technical publications resulted.

At about this time it was decided to initiate work in plant physiology in the Bureau of Science at Manila, and the undersigned made a survey of available candidates, the result being the selection of Dr. Brown for appointment in the Philippine service. It was in Manila, in a decidedly stimulating, even although a tropical environment, that Dr. Brown established himself as a productive scientist, for his work there added distinctly to the prestige of the small group of individuals on whose shoulders fell the responsibility of developing and maintaining the scientific work fostered and supported by the Philippine Government.

It soon became apparent that Dr. Brown's interests were by no means confined to plant physiology, and gradually he entered the field of ecology, the result being the publication in 1919 of his monographic "Vegetation of Philippine Mountains," based on a long, arduous and critical series of field studies in the primary forests of Mount Maquiling. He retained his Bureau of Science appointment from 1911 to 1923, but in this period acted as associate (later professor) of botany, in the University of the Philippines from 1919 to 1924, and as chief of the Division of Investigations in the Philippine Bureau of Forestry from 1919 to 1920.

His teaching experience led him into the text-book field, for he soon found that there were no properly balanced botanical text-books available for instruction in the subject for students resident in the tropics. Most texts had previously been prepared by individuals familiar from long residence with the vegetation of the temperate zone, but with little or no tropical experience. The result of Dr. Brown's efforts here was his very excellent "Textbook of General Botany," published in 1925, a text characterized by its balance, remarkable for its excellent illustrations and for its adaptability to the actual teaching of the subject in any climate. Ten years later this was followed by his equally excellent and authoritative "Plant Kingdom."

With an active and inquiring mind, fully at home in several diverse fields of botanical science, including plant physiology, ecology, morphology and economic botany, for in the latter field Dr. Brown was also a productive worker, his actual botanical output was limited for the next nine years, from 1924 to 1933, for in the former year he was selected to succeed the undersigned in the distinctly exacting position as director of the Bureau of Science in Manila. Here he proved himself as an administrator, his work involving the general supervision of an enormously wide range of subject-matter as well as the editorship of the *Philippine Journal of Science*. In this position Dr. Brown's period of service was longer than that of any of his three predecessors, except that of the first incumbent, Dr. Paul C. Freer.

Retirement from administrative work and from the Philippine service in 1933 gave Dr. Brown the opportunity of devoting practically full time to the advancement of research in the field that now claimed his attention, that of general morphology, with special reference to the significance of the floral nectaries as indicators of broad relationships of the major groups of plants. He elected to remain in Manila after his retirement from the government service, where he had access to a wealth of fresh material essential to the proper prosecution of his special studies. As the work developed he commenced to feel the need of access to other than tropical types, and in the latter part of 1936 correspondence was initiated between himself and the late Dr. Duncan S. Johnson, tentative plans being then made for him to locate in or near Baltimore or Washington, where he could have access to ample herbarium and library facilities. At the time of Dr. Johnson's death in February, 1937, laboratory space had been made available to Dr. Brown in Johns Hopkins University. It was then learned that Dr. Brown was about ready to transfer his botanical activities from the Philippines to the United States, whereupon he was offered a lectureship in botany at Johns Hopkins University. He took up his residence in Baltimore in February, 1938, having charge of the botanical laboratory and of the botanical garden at the university.

Here in addition to his teaching duties he concentrated on his studies of the significance of the floral nectaries, having in mind the ultimate production of a major work, planned to cover all possible groups (families) of flowering plants. His untimely death leaves this culminating task incomplete, although it is hoped that ways and means may be devised to continue the work.

Dr. Brown's botanical interests were unusually wide, and he fortunately had exceptional opportunities available to him through a very long period of service in a tropical environment. Taking advantage of these opportunities, his published results were uniformly excellent, no matter in what field he worked. He was a member of numerous organizations, including the American Ecological, Meteorological and Botanical Societies, a fellow of the American Association for the Advancement of Science and a member of Phi Beta Kappa. He married Mary Angus Blythe in Manila, on June 3, 1927, who with two sons survive him. His loss is a serious one to America and to world botany.

E. D. MERRILL

RECENT DEATHS AND MEMORIALS

DR. CHARLES SKEELE PALMER, consulting chemical engineer, inventor of a gasoline-cracking process that separated mineral oil into gasoline, fuel oil and gas, previously professor of chemistry at the Univer-

ity of Colorado, died on November 30 at the age of eighty-one years.

PROFESSOR FREDERICK NEWTON WILLSON, emeritus professor of descriptive geometry, stereotomy and technical drawing at Princeton University, died on November 15. He was eighty-three years old.

PROFESSOR R. V. WHEELER, professor of fuel technology in the University of Sheffield, died on October 28 at the age of fifty-three years.

DR. WILFRED TROTTER, professor of surgery at the University College Hospital Medical School and surgeon to the University College Hospital, London, died on November 25 at the age of sixty-seven years.

A PORTRAIT of the late Professor Henry Smith, formerly dean of the School of Mines of Columbia University, painted by H. E. Ogden Campbell, was unveiled in the Low Memorial Library on November 27.

A MEETING dedicated to the memory of Dr. William Hallock Park, emeritus professor of medicine in the New York University College of Medicine until his retirement in 1936 and director of the Bureau of Laboratories of the New York City Department of Health, was held on November 28 at the New York Academy of Medicine. The speakers included: Mayor La Guardia; Dr. Harry Woodburn Chase, chancellor of New York University; Dr. Malcolm Goodridge, president of the academy; Dr. Anna W. Williams, formerly assistant director of the Health Department Bacteriology Laboratories under Dr. Park, and Dr. Augustus B. Wadsworth, director of laboratories and research for the New York State Department of Health.

SCIENTIFIC EVENTS

ENGINEERING EDUCATION

A REPORT on "Present Status and Trends of Engineering Education in the United States," by Dr. Dugald C. Jackson, emeritus professor of engineering at the Massachusetts Institute of Technology, has been issued by the Engineers' Council for Professional Development, with the aid of funds supplied by the Carnegie Foundation for the Advancement of Teaching. The report is one of the valuable by-products of the task of accrediting curricula in engineering undertaken by the Committee on Engineering Schools of the Engineers' Council for Professional Development.

Dr. Jackson's report may be divided roughly into four parts. An appendix has been provided by Allen W. Horton, Jr., who acted as secretary to the committee during the period in which the accrediting procedure was developed and put to the test, and the data collected. In the early chapters of the report Dr. Jackson traces the history of developments that led up to the accrediting program, summarizes the well-known Mann, Wickenden and Potter reports that have played important roles in that development, and sketches briefly the status of engineering education in America in 1939. He next turns his attention to the Committee on Engineering Schools of the Engineers' Council for Professional Development, to the procedure it adopted in its task of accrediting curricula and to comments on some of the perplexing problems it had to face and the progress of the committee's own thinking and methods that resulted from actually coming to grips with these problems.

The data themselves, which cover 679 curricula in 139 institutions, assembled, coordinated and analyzed in the form of tables and charts, with Dr. Jackson's comments, occupy the third portion of the report. These data were gathered for the purpose of the accrediting program, which they usefully served, but they constituted a store of information of value to engineers and educators, and were so fruitful for the improvement of engineering education that the committee was able to secure from the Carnegie Foundation for the Advancement of Teaching the funds necessary to put them in shape for public use.

As to the present status, Dr. Jackson provides a convenient summary in the following passages quoted from the report:

> It is reasonable to say that the majority of the substantially one hundred and sixty engineering schools in the United States are now in a sound status and are wide-awake to improve their effectiveness. The principal defects in the quality of faculties are perhaps a lack of recognition of the unity of learning in science and in political economy as applied in engineering, an inadequate espousal of professional ideals as distinguished from either craftsmanship or speculative philosophy, a failure to impress on all students that a successful engineer's life demands continuous study throughout its length, and a failure to dovetail the curricula into political economy on one side as thoroughly as they are dovetailed into physical science on the other. . . . Part of the onus for the defects named may be appropriately laid at the doors of administrative officers. . . . There is an additional fault . . . which is the failure to recognize that the proper use of research vitalizes all levels of engineering education, from the sophomore undergraduate level to the most advanced levels, which makes it a requisite and important factor in such education.

THE ALASKA FISHERIES EXPERIMENTAL COMMISSION

AN Alaska Fisheries Experimental Commission has

been organized with an appropriation from the Legislature of $20,000 for cooperation in the establishment of a fishery products laboratory in Alaska.

The members of the commission are the governor of Alaska, Dr. Ernest Gruening; J. W. Mendenhall, of Ketchikan, member for industry, and Seton H. Thompson, member for the bureau. At a meeting on August 20 Governor Troy, who has since resigned, was elected chairman and Mr. Mendenhall, secretary. It was then decided to enter into a cooperative agreement with the U. S. Bureau of Fisheries for the operation of the laboratory.

At this meeting it was also decided to establish the office of the commission at the laboratory building in Ketchikan, when constructed, and Mr. Mendenhall was designated as liaison officer with authority to consult appropriate officials of the Bureau of Fisheries regarding construction, maintenance and operation.

A site has been selected on which to construct the laboratory, and the sum of $50,000 has been allocated for this purpose by the Public Works Administration. The building will be approximately 60,000 cubic feet in size.

The laboratory will serve as headquarters for the Alaska technical and economic research staff, who will conduct studies on the capture, preservation and marketing of Alaska fishery products.

In general, it is proposed to conduct research along the following lines:

Improvement of processes and methods of capture, handling and preserving of species now utilized.

Development of new methods for processing species now utilized.

Preparation of useful commodities from species not utilized.

The purpose of this work will be to extend the processing or fishing season over a longer period of the year. At present most of the fishing and packing business is done in the summer.

THE BIOLOGICAL RESEARCH DIVISION OF THE EDMUND NILES HUYCK PRESERVE

THE Edmund Niles Huyck Preserve at Rensselaerville, Albany County, New York, was incorporated in 1931. The purpose of the preserve, as outlined in the certificate of incorporation, is to

preserve the natural beauty of Rensselaerville Falls, Lake Myosotis, Lincoln Pond and the lands around them in the town of Rensselaerville; to increase the general knowledge and love of nature, particularly that of trees and wildlife, by maintaining a demonstration of reforesting and forest culture, and by providing means for increasing and protecting the birds, wild animals and fish within the boundaries of said land.

The preserve covers nearly a square mile of diversified habitats. Two lakes, one of eighty acres, numerous streams, dense beech-hemlock stands and arable fields provide a diverse attraction for the naturalist. The elevation is 1,650 feet above sea. As a preliminary step to the possible establishment of a biological station on the preserve a study of the biota was made during the summers of 1937 and 1938.

Three fellowships (two of three months each and one for the entire year) have been provided, the recipients to conduct basic zoological investigations in the field of animal behavior or ecology. Donald Griffin, of Harvard University, and Dr. E. C. Raney, of Cornell University, were awarded the 1939 summer fellowships. Dr. Eugene P. Odum, a graduate of the University of Illinois, has accepted the post of resident naturalist for 1940.

Members of the Scientific Advisory Committee are Dr. W. J. Hamilton, Jr., *chairman;* Dr. Lewis A. Eldridge; Dr. John R. Greeley; Dr. G. Kingsley Noble; Dr. Thomas Ordway and William Vogt. Inquiries regarding the Biological Research Division should be addressed to W. J. Hamilton, Jr., Cornell University, Ithaca, New York.

AWARDS OF THE ROYAL GEOGRAPHICAL SOCIETY

THERE have already been given in SCIENCE the names of those who received the awards of the Royal Geographical Society at the annual meeting in London on June 26. The citations made by Field Marshal Sir Philip Chetwode, president of the society, follow:

With the approval of His Majesty, the Founder's Medal has been awarded to Mr. Arthur M. Champion. Mr. Champion has spent thirty years in East Africa, largely in the administrative service of Kenya. For some years he was in administrative charge of the Turkana Province. On his appointment, Mr. Champion made it his duty to carry out the first systematic survey of the Province on a trigonometrical framework, producing a valuable map in six sheets on the scale of 1/250,000. In addition to this he investigated the physical geography and geology of the area, and more particularly of Teleki's Volcano and the lava fields south of Lake Rudolf. He has communicated the results of his work in valuable papers to the society, and has recently shown to us the film which he made on a motor journey across Africa from Cape Verde to Nairobi, carried out after he had retired from the Colonial Service. Mr. Champion has now made his home in Kenya, and we look forward to further contributions from him on the geography of East Africa.

His Majesty the King has approved of the award of the Patron's Medal to Professor Hans Ahlmann, of the University of Stockholm, for his exploration and glaciological studies in the Arctic. He has specialized in studying the work of ice and snow and for this purpose he organized and led the two Swedish-Norwegian expeditions to Spitsbergen in 1931 and 1934, and the Swedish-Icelandic expedition to Vatnajökull in 1936–37. The many important

scientific monographs resulting from these expeditions have been noticed from time to time in the *Geographical Journal*, and we have had the pleasure on a former occasion of hearing a paper by him upon the physical characteristics of glaciers. Professor Ahlmann's work has stimulated much interest in this important branch of our science, and younger explorers and students owe a great deal to his encouragement and assistance. He is leaving in a few weeks' time to continue his researches in northeast Greenland.

The Murchison Grant has been awarded by the council to Mr. Robert Bentham for his surveys and geological investigations in Ellesmere Land. Mr. Bentham first went to the Arctic with the Oxford University Exploration Club's Ellesmere Land Expedition in 1934. In 1936 he returned by himself to the police post at Craig Harbour, Jones Sound, where he spent two years making a plane-table survey of southeast Ellesmere Land and in geological and archeological work. He also made an extended journey to the northwest.

The Back Grant has been awarded by the council to Lieutenant-Commander R. E. D. Ryder, R.N., for his captaincy of the *Penola* and his marine surveys on the British Graham Land Expedition. Commander Ryder's achievement in navigating the *Penola* in high latitudes and often in uncharted waters, with a crew which had little nautical experience before leaving England, was a fine feat of resourceful seamanship. He also took every opportunity of extending our hydrographical knowledge of the island-strewn waters and coasts of western Graham Land, and his surveys have been incorporated in the official charts. Commander Ryder being absent on duty, I shall ask his father, Colonel Ryder, to accept the award on his behalf.

The Cuthbert Peek Grant has been awarded by the council to Mr. W. V. Lewis for his physiographical studies in Great Britain and Iceland. Mr. Lewis, who is university demonstrator in geography at Cambridge, has taken part in one expedition and led another to Iceland. His interests are chiefly in the evolution of glacial features and of shorelines and he had also pursued these studies in Great Britain. At various times he has imparted to us the results of his observations on Dungeness Foreland, the Chesil Beach and elsewhere on the English coast, as well as upon the coast of southeast Iceland.

The council has awarded the Gill Memorial to Mr. J. V. Harrison for many years' exploration in Central and South America and southern Iran. Mr. Harrison, who is a geologist by training, saw active service during the war with the Royal Engineers in Mesopotamia. Since then he has been engaged on topographical and geological surveys in Iran, Mexico, Venezuela, Colombia, Honduras and the West Indies. In particular he has described to the society his journeys and surveys of the mountainous and inhospitable Bakhtiari and Kuhgalu country in southwestern Iran, formerly difficult of access to travelers and unsurveyed, the homes of restless tribes. Mr. Harrison's work has not only provided us with our first precise knowledge of the topography of these regions, but has also contributed to the elucidation of some major problems of the earth's structure. He is now at work in the Central Andes of Peru, and I shall ask Dr. G. M. Lees to accept this award on his behalf.

SURVEY OF RESEARCH IN INDUSTRY

THE appointment of Raymond Stevens, vice-president of Arthur D. Little, Inc., of Cambridge, Mass., as director of a nation-wide survey of research in industry which is to be started at once, has been announced by Dr. Ross G. Harrison, chairman of the National Research Council. The announcement followed the first meeting of a special committee held at the Engineers' Club in New York City to formulate initial plans. Mr. Stevens has obtained leave of absence that will permit him to devote a principal portion of his time to the survey, the headquarters of which will be in the National Research Council Building in Washington. He is known as an authority on the organization of large-scale research programs, as well as the application of research for the solution of specific problems in industry.

In announcing the appointment, Dr. Harrison stated that while funds for the work had been made available by the National Resources Planning Board, of which Frederic A. Delano is chairman, the survey would be conducted and the report prepared by the National Research Council. This is in accordance with plans approved by an advisory committee of leading scientific men, industrial research directors and executives, of which F. W. Willard, president of the Nassau Smelting and Refining Company, New York, is president. The report will be submitted in printed form by the council next year and will present "an objective study of industrial research as a national resource, as a means of aiding in its further development and utilization."

The National Research Council is composed largely of the accredited representatives of about eighty-five national scientific and technical societies. It was established in 1916 at the request of President Woodrow Wilson, by the National Academy of Sciences, to coordinate the research facilities of the country for work on war problems involving scientific knowledge. An executive order by President Wilson in May, 1918, complimented the National Academy and the National Research Council on war services and requested that the academy perpetuate the National Research Council with six peace-time objectives: to stimulate research in natural sciences for national defense and public welfare; to survey larger possibilities and formulate comprehensive research projects; to promote cooperation in research at home and abroad; to promote active cooperation with War and Navy Departments and civil branches of the government; to direct attention of scientific workers to war problems and to make available scientific information at home and abroad in cooperation with other agencies.

SCIENTIFIC NOTES AND NEWS

DR. JULIAN HUXLEY, secretary of the Zoological Society, London, was the guest of honor on December 2 at a dinner arranged by the Smithsonian Institution, the American Association for the Advancement of Science and *The Scientific Monthly*. Dr. Forest Ray Moulton, permanent secretary of the association, presided. Remarks were made by a representative of the Marquis of Lothian, the British Ambassador, who was unable to be present, and by Dr. Charles G. Abbot, secretary of the Smithsonian Institution. Dr. Isaiah Bowman, president of the Johns Hopkins University, introduced Dr. Huxley, whose address was entitled "Science, Social and Unsocial."

DONALD WILLS DOUGLAS, president of the Douglas Aircraft Company, Santa Monica, Calif., has been awarded by the Institute of the Aeronautical Sciences the Daniel Guggenheim Medal for 1939 "for outstanding contributions to the design and construction of transport airplanes."

THE Lamme Medal of the Ohio State University was presented to Thomas Alvin Boyd, since 1923 head of the fuel department of General Motors Research Laboratories, who was the codiscoverer of anti-knock effects of liquid lead compounds, at a dinner of the fourth annual Industrial Research Conference.

FREDERICK SKENE, who for eighteen years has been dean of the School of Technology of the College of the City of New York, was the guest of honor at a reception by the Engineering Alumni on November 29 at the City College Club.

FRANCIS P. GARVAN, JR., has been elected *president* of the Chemical Foundation, an office held by his father, the late Francis P. Garvan, from the formation of the foundation until his death in 1937. George J. Corbett was elected *vice-president;* William M. Buffum, *treasurer,* and Edward J. Muhs, *secretary.*

CERTIFICATES of honorary membership in the American Society of Mechanical Engineers were presented at the sixtieth annual meeting, which opened in Philadelphia on December 4, to Dexter Simpson Kimball, dean-emeritus of the College of Engineering, Cornell University; to Edwin Jay Prindle, retired patent attorney and mechanical engineer, East Orange, N. J.; to Charles T. Main, industrial engineer and expert on power and textile plants, Boston, Mass., and to Henry Hague Vaughan, consulting engineer and president of the Canadian Foreign Investment Corporation, Montreal, Canada.

DR. WILDER PENFIELD, director of the Montreal Neurological Institute and professor of neurology at McGill University, has been elected president of the Royal College of Physicians and Surgeons of Canada.

THE degree of doctor, *honoris causa,* has been conferred by the faculty of medicine of the University of Bordeaux on Dr. Constantin Daniel, professor of obstetrics and gynecology at the University of Bucharest. The diploma and the insignia were handed to him in the presence of the deans of the university and of prominent citizens.

DR. NAGAMICHI KURODA, an authority on the birds of Japan and eastern Asia, has succeeded to the title of Marquis Kuroda previously held by his father, who died last August at the age of seventy-two years.

ACCORDING to the *Australian Journal of Science,* the title of emeritus professor has been conferred by the senate of the University of Sydney on Dr. J. Douglas Stewart, who recently retired from the chair of veterinary science at the university. Professor Stewart was the first professor of veterinary science at Sydney, and served for thirty years as dean of the faculty.

DR. W. ALBERT NOYES, JR., has been appointed head of the department of chemistry of the University of Rochester. He succeeds Professor Victor J. Chambers, who has become professor emeritus.

DR. HARRY STACK SULLIVAN, chairman of the faculty of the Washington School of Psychiatry, has been appointed professor of psychiatry and director of the department of psychiatry and neurology at the Georgetown University School of Medicine. He succeeds the late Dr. Daniel Percy Hickling, who was a member of the faculty for more than forty years.

Industrial and Engineering Chemistry reports that Jules Bebie, for a number of years director of research at the Monsanto Chemical Company, has been appointed lecturer in chemical engineering at Washington University, St. Louis.

ERWIN H. AMICK has resigned his position with the Standard Oil Development Company to become an assistant professor in chemical engineering at the University of Pennsylvania.

SIR ROBERT KELLY, from 1922 to 1939 professor of surgery at the University of Liverpool, has retired with the title emeritus.

DR. RICHARD VAN DER RIET WOOLLEY has been appointed director of the Commonwealth Solar Observatory at Mount Stromlo, Australia. Dr. Woolley was chief assistant at the Royal Observatory, Greenwich, from 1933 to 1937, and since then has been John Couch Adams astronomer in the University of Cambridge. He has been editor of *The Observatory* since 1933.

DR. ELMER O. KRAEMER, formerly connected with the Experimental Station of E. I. du Pont de Nemours and Company, has recently returned from Europe, where he spent a year as fellow of the Lalor Foun-

dation, continuing his researches on the sizes and shapes of giant molecules with Professor The Svedberg at the University of Upsala, Sweden. Dr. Kraemer is now associated with the Biochemical Research Foundation of the Franklin Institute in Philadelphia.

DR. CHARLES O. WARREN, JR., instructor in physiology at Cornell University Medical College, has been awarded a grant from the Committee on Scientific Research of the American Medical Association for the continuation of studies on the metabolism of bone marrow. A renewal has been made of the grant of last year to Dr. Joseph H. Roe, professor of biochemistry in the School of Medicine of the George Washington University, in support of the continuance of his work on methods for the determination of ascorbic acid and of a study of the effect of vitamin C upon gastric function.

DR. IRVINE MCQUARRIE, head of the department of pediatrics at the Medical School of the University of Minnesota, has leave of absence. He plans to spend six months as visiting professor of pediatrics at the Peiping Union Medical College. He will leave for China early in January.

ACCORDING to *The Harvard Alumni Bulletin*, Dr. Lewis W. Hackett, who represents the International Health Division of the Rockefeller Foundation in the Mediterranean region, has moved from Rome to Egypt. His address after January 30 will be the Public Health Laboratories, Cairo.

HARLAN B. HOLMES returned to the service of the Bureau of Fisheries in October after a four-year period of detail to the War Department, during which time he designed the fishways at Bonneville Dam and supervised the initial period of their operation. Mr. Holmes now assumes charge of the recently established Hydraulics Section of the Division of Scientific Inquiry. Associated with Mr. Holmes in the Hydraulics Section is O. W. Lindgren, associate hydraulic engineer, who has recently been engaged in directing the installation of screens at various federal irrigation projects in the Northwest.

DR. WILLIAM M. MANN, director of the National Zoological Park, Washington, D. C., lectured on November 30 to an audience numbering over eight hundred before the Lancaster Branch of the American Association for the Advancement of Science. He described the work accomplished by the National Geographic Society-Smithsonian Expedition of 1937 in the Dutch East Indies.

PROFESSOR DOUGLAS JOHNSON, of Columbia University, gave an illustrated lecture on "The Physical History of the Grand Canyon District" before the students and faculty of the Connecticut College on October 31. On December 7 he addressed the Geology Society of the College of the City of New York on "The Supposed Meteorite Craters of the Carolina Coast."

DR. F. F. NORD, of Fordham University, editor of *Ergebnisse der Enzymforschung*, lectured under the auspices of the Research Council at the Iowa State College on November 27 and 28, on "Low Temperature and Its Relation to Colloid Chemistry" and on "The Enzyme System of Fusaria and Its Action." At a meeting of Sigma Xi he spoke on "The Modern Concepts of the Mechanism of Alcoholic Fermentation."

DR. GEORGE JOBBERNS, head of the department of geography of the Canterbury University College, Christchurch, New Zealand, is a visiting scholar in geomorphology at Columbia University during the current semester. In November he delivered a course of four illustrated lectures on "The Geology of New Zealand," under the auspices of the department of geology. On November 28 he gave an illustrated lecture on New Zealand Landscapes, under the auspices of the Columbia Institute of Arts and Sciences.

THE Croonian lecture of the Royal Society was delivered by Professor J. Gray at the department of zoology of the University of Cambridge on November 16. His subject was "The Aspects of Animal Locomotion."

ACCORDING to *The Fisheries Service Bulletin*, Leo D. Sturgeon, Foreign Service Officer of the Department of State on detail in the department, has been assigned to serve as assistant to Counselor R. Walton Moore. The primary duty of Mr. Sturgeon is to assist in the formulation of policy and in the coordination of action in the State Department on international aspects of fishery matters. This will involve the study and handling of problems concerning methods of regulating the fisheries and the formulation of arrangements for the conservation of international fisheries of concern to American interests. Mr. Sturgeon will act as liaison officer between the Department of State and other government agencies.

THE *Journal* of the American Medical Association reports that members of the state board of examiners in the basic sciences for Florida include the following recently appointed by the governor: Dr. Mark Wirth Emmel, professor of veterinary science, University of Florida, *chairman;* Dr. John Ferguson Conn, professor of chemistry, the John B. Stetson University, *secretary;* Dr. Ezda May Deviney, professor of zoology, Florida State College for Women; Dr. Jay F. W. Pearson, professor of zoology, University of Miami, and Dr. Donald D. Bodé, professor of chemistry, Tampa University.

DR. A. O. WEESE, professor of zoology in the Uni-

versity of Oklahoma, was elected president of the board of directors of the newly incorporated Grassland Research Foundation at a meeting held in Norman, Okla., on November 7. Other officers are G. W. Goldsmith, professor of botany at the University of Texas, and V. E. Shelford, professor of zoology at the University of Illinois, *vice-presidents;* J. M. Aikman, professor of botany at Iowa State College, *secretary;* and Mrs. M. W. Shackleford, professor of biology at the Oklahoma College for Women, *treasurer*. Incorporation of the group has been completed under the laws of Oklahoma. Membership, however, includes those living in the grassland area as far distant from Oklahoma as Saskatchewan, Oregon, Arizona, Texas and Illinois. A meeting of the corporation will be held in Columbus, Ohio, during the Christmas vacation, as part of the meeting of the American Association for the Advancement of Science. The Grassland Research Foundation is the outcome of the work of the committee on ecology of the grasslands of the National Research Council.

FOR the positions in the Bureau of Animal Industry, Department of Agriculture, of protozoologist at a salary of $3,800 a year, of associate protozoologist at a salary of $3,200 a year and assistant protozoologist at a salary of $2,600 a year, applications must be on file with the U. S. Civil Service Commission at Washington, D. C., not later than January 2. Vacancies in positions requiring similar qualifications will be filled from these examinations, unless it is found in the interest of the service to fill any vacancy by reinstatement, transfer or promotion. The salaries named above are subject to a deduction of 3½ per cent. toward a retirement annuity. Separate lists of eligibles will be established in each of the above grades in: (1) Coccidiosis; (2) parasitic protozoa of the blood; (3) general parasitic protozoa. Permanent employees in the classified service will, upon earning a passing mark in these examinations, have their names placed upon a separate list of eligible government employees, which list may be certified separately to fill appropriate vacancies in accordance with the civil-service rules.

DR. ERNEST CARROLL FAUST, secretary of the American Academy of Tropical Medicine, reports that the sixth annual session of the academy was held in conjunction with the American Society of Tropical Medicine meeting with the Southern Medical Association at Memphis, Tenn., on November 23. The presidential address was delivered by Dr. W. W. Cort, of the Johns Hopkins University, on the subject "Research on Helminth Diseases and Public Health Progress." The second presentation of the Theobald Smith Gold Medal of the George Washington University for distinguished work in tropical medicine was presented by Dr. Alfred C. Reed, of the University of California, for the academy, to Dr. Richard P. Strong, of the Harvard Medical School. At the business session of the academy, the officers elected were: Admiral Charles S. Butler, *president;* Dr. Marshall A. Barber, *vice-president;* Dr. Ernest Carroll Faust, *secretary;* Dr. Thomas T. Mackie, *treasurer;* Colonel George R. Callender, *councillor*. Five new members were elected, and Dr. L. O. Howard, member, was elected to honorary membership. It was voted to hold the seventh annual session of the academy with the American Society of Tropical Medicine at Louisville, Ky., in November, 1940.

ACCORDING to the *Journal* of the American Medical Association, the Milwaukee Academy of Medicine and the Marquette University School of Medicine have consolidated their medical libraries, forming a collection of 34,000 volumes. Dr. Irving S. Cutter, dean of Northwestern University Medical School, Chicago, was the speaker at the ceremony inaugurating the new library on October 17. Facilities have been enlarged at the university to receive the academy's library, the most important part of which is the collection of the late Dr. Horace Manchester Brown.

DISCUSSION

HEAVY WATER AND LONGEVITY

THE suggestion by Barnes[1] that deuterium oxide would be found to retard life processes, thus favoring longevity, was predicated upon the lower energy content of deuterium as compared with hydrogen.

The undersigned[2] have shown, during the past summer, that heavy water retards four chief growth activities of *obelia geniculata*. This is a sessile marine animal living in colonies of a few millimeters length. Forty-six experiments on 27,000 animals were made with concentrations up to 10 per cent. D_2O. The results accord with the general trend of observations by others on the growth of various low forms of life[3] and can best be interpreted on the assumption that deuterium oxide blocks anabolism. Since the evidence concerning regressive and senile stages of obelia also favors retardation rather than acceleration by D_2O, the prolongation of individual existence in these animals appears established.

While our results, as far as they go, fulfill the prediction of Barnes, they do not contribute convincingly

[1] T. C. Barnes, *Jour. Am. Chem. Soc.*, 55: 4332–4333, 1933.

[2] F. S. Hammett and H. G. Barbour, *Growth*, 3: 4, 1939.

[3] See reviews: S. L. Meyer, *Jour. Tenn. Acad. Sci.*, 10: 111–115, 1935; H. G. Barbour, *Yale Jour. Biol. Med.*, 9: 551–565, 1937; C. B. Davenport, *Ann. Rev. Physiol.*, 1: 81–108, 1939.

to the question of mammalian longevity. The retarding effects of D_2O on the growth of mice bearing tumor transplants were demonstrated by Barbour and Allen.[4] One fifth saturation with deuterium oxide retarded the growth of both tumors and hosts, the latter showing shorter survival periods than the H_2O controls. A number of other mice have for several months tolerated one fifth saturation with D_2O, without evidence for enhanced longevity.

More significant is the fact that while the obelia offers evidence for decreased catabolism in low forms of animal life, mammals respond to one fifth saturation of deuterium oxide by catabolic stimulation persisting for many days.[5] Such difference in mammals may be attributable to checks and balances acquired in their phylogenetic development, as are, for example, provided by the elaboration of hormones. Now, deuterium oxide, presumably by providing a slow-acting form of hydrogen, protects and "prolongs the life" of at least two of these unstable hormones, namely, epinephrine[6] and acetylcholine.[7] The first of these has been found responsible for the metabolic increases, up to +20 per cent., which tend to make the mice "live faster" rather than slower.

Therefore, although deuterium oxide retards growth and anabolism and in toxic concentrations even delays catabolism in all forms of life so far examined, it is not to be expected that mammals enjoying the luxury of partial saturation with this substance will exhibit enhanced longevity.

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HEPARIN AND BLOOD CLOTTING

THERE recently appeared an article in which Astrup[1] confirmed our observation[2] that normal plasma contains an unknown factor, which, in conjunction with heparin, blocks the transformation of prothrombin into thrombin. Both his work and ours showed that heparin alone has little or no effect in blocking this reaction—a finding which conforms to the earlier experiments of Mellanby[3] and Quick.[4] However, in mixtures containing both the plasma factor and heparin, our work and that of Astrup showed that marked inhibition of thrombin formation results.

In a recent note in this column, Ferguson[5] discussed these results, and indicated, erroneously, we believe, that Howell and Holt's[6] original work had brought out all these same facts. It is true that they did find that the *destruction* of thrombin by heparin requires a plasma factor ("pro-antithrombin"), but they believed that heparin interfered *directly* with the conversion of prothrombin into thrombin (antiprothrombic action of heparin). Our work and that of Astrup has brought out the new concept that a plasma factor is needed for this inhibitory action of heparin.

Although we have suggested that this new plasma factor and the pro-antithrombin of Howell may be identical chemically, as yet no data are available on this point and the question must be left for future work.

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MASTODON REMAINS FOUND IN WEST VIRGINIA

ON Monday, October 9, there was brought to the biological laboratories of Bethany College the proximal portion of a long bone, too large to be that of any local domesticated animal. This bone fragment had been uncovered and picked up by a Mr. Funk, the operator of a steam shovel engaged in stripping coal about two miles west of Bethany, W. Va., in Brooke County, on a tract of land known as the Pendleton Farm and owned by a Mr. Petzol, of Hollidays Cove, W. Va.

The undersigned went immediately to the stripping operation and there found a number of other fossilized bones, as well as a portion of a tooth. These materials were removed to the biological laboratories of Bethany College. Dr. Leroy Kaye, paleontologist of the Carnegie Museum, Pittsburgh, Pa., was called into consultation and it was agreed that these were parts of a skeleton of the American mastodon.

The skeleton remains were found in a deposit of blue clay about 18 feet below the surface. This layer of clay was 6′ 3″ in thickness. It was probably a Pleistocene deposit. This layer contained an abundance of Gasteropod and Pelecypod fossils, as well as numerous pieces of fossilized wood. Overlying this was another layer of yellow clay of a gravelly nature,

[1] T. Astrup, SCIENCE, 90: 36, 1939.
[2] K. M. Brinkhous, H. P. Smith, E. D. Warner and W. H. Seegers, *Am. Jour. Physiol.*, 125: 683, 1939.
[3] J. Mellanby, *Proc. Roy. Soc. B.*, 116: 1, 1934.
[4] H. G. Barbour and E. Allen, *Am. Jour. Cancer*, 32: 440–446, 1938.
[5] H. G. Barbour and L. E. Rice, *Jour. Pharm. Exp. Therap.*, 62: 292–300, 1938.
[6] H. G. Barbour, Internat. Physiologen-Kongr., 16, Zurich, 1938, *Kongressber.*, pt. 2, 34–35.
[7] H. G. Barbour and V. C. Dickerson. *Jour. Pharm. Exp. Therap.*, 65: 281–286, 1939.

[4] A. J. Quick, *Proc. Soc. Exp. Biol. and Med.*, 35: 391, 1936.
[5] J. H. Ferguson, SCIENCE, 90: 272, 1939.
[6] W. H. Howell and E. Holt, *Am. Jour. Physiol.*, 47: 328, 1918.

approximately 11′ 6″ in thickness; both overlay a thick stratum of shale above a vein of Pittsburgh coal.

A study of the geology of the region revealed that in the geological past the bed of clay formed the bottom of an ancient stream bed. Fortunately the mining operations cut across the strata, thus revealing the geological history quite definitely.

The portions of the skeleton recovered thus far consist of the heads of both femurs, the proximal end of the humerus, a practically complete right scapula, a number of foot and toe bones, together with portions of the vertebra. A number of other bony fragments are in the laboratories and will be assembled later.

Two large fragments of a molar were found and these have been fitted together. The figuration of the tooth and the marks established the identity of this animal definitely as a mastodon.

To the best of our knowledge this is the first report of the finding of mastodon remains in this section of the State of West Virginia. Thirty-seven years ago a portion of a tusk was found in a gravel pit near Brilliant, Ohio, eight miles west of Bethany, W. Va., on the west bank of the Ohio River.

It is planned to continue the search in the region of the original find and make a more detailed report at a later date.

W. J. SUMPSTINE
B. R. WEIMER

BETHANY COLLEGE (W. VA.)

BORGMEIER'S REVISTA DE ENTOMOLOGIA. AN APPEAL TO ENTOMOLOGISTS

IN the field of entomology, many of us have depended for years on foreign journals, the channels for publication being wholly inadequate in this country. I notice, in my case, that in 1938 nearly half of my papers were published abroad. In the near future, some of the European periodicals will be completely closed to us, while others plan to carry on on a modest scale or even to suspend for the duration of hostilities. It seems most opportune to call the entomologists' attention to a New World publication, which, with the proper support of American workers, may well prove the ideal solution to our present difficulties. Started in 1931, the *Revista de Entomologia,* of Rio de Janeiro, is now running through the tenth volume, and has kept up an unequaled standard of excellence. Each of the nine completed volumes covers some 500 pages, adequately illustrated with text-figures and half-tone plates. The papers are cosmopolitan in authorship (being written in English, German, French, Spanish and Portuguese) and cover practically every phase of entomology, theoretical as well as practical. Each issue, of which there are now three to a yearly volume, concludes with an extremely valuable critical bibliography of neotropical entomology. This feature alone makes the *Revista* indispensable to all students of Central and South American insects. From the start, the *Revista* has been conducted as a labor of love by Father Thomaz Borgmeier, O.F.M., an entomologist of repute in his own field. As most European subscribers are likely to drop out at present, it is to be feared that the editor will run into some unexpected difficulties. All American entomologists are urged to rally to his support. Beginning next year, Father Borgmeier plans to accept for publication papers dealing with North American insects also. The editor's address is Convento S. Antonio, Largo da Carioca, Rio de Janeiro, Brazil.

J. BEQUAERT

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SCIENTIFIC BOOKS

MEDICAL CLIMATOLOGY

Medical Climatology. By CLARENCE A. MILLS. 296 pp. Baltimore, Md.: Charles C Thomas. 1939.

MILLS's "Medical Climatology" is symptomatic of a movement which may become a mighty tide a generation hence. For two generations or more biological investigation has centered upon the organism itself far more than upon its environment. The structure of the cell, the mechanism of inheritance, the chemical composition of glandular secretions and the influence of bacteria and other internal parasites have engrossed attention. As a result not only have the ravages of infectious diseases diminished greatly, but new and valuable varieties of domestic plants and animals have been produced in great numbers. This progress, however, has gone hand in hand with comparative neglect of the other side of the shield. Our knowledge of how the organism is influenced by the external environment represented by climate, soil and so forth is still pitifully small. The botanists, to be sure, have recently made good progress in ecology, but only the merest beginning has been made in studying the ecology of animals and man. The significance of "Medical Climatology" lies in the fact that it opens up many new lines of approach to the fruitful field of human ecology.

The thesis of the book is that two main types of disease—infectious and degenerative—display opposite relations to climate. The basic reason for this, as Mills sees it, is that human metabolism varies greatly in response to weather and climate. Warm and monotonous climates lower the rate of metabolism; thus diminishing people's power to resist all sorts of infections. Cold and variable climates increase metabolism,

us making people active, energetic and able to resist fection. Unfortunately, however, this metabolic acity places too great a strain upon the vital organs, us leading to degenerative diseases of the heart, dneys, nervous system, and so forth. Hence in rm, mild, enervating climates, infectious, parasitic seases are especially common, whereas in cool, varile and stimulating climates degenerative diseases e dominant. Recent medical progress has greatly minished the danger from infectious diseases, such tuberculosis, diphtheria, measles, yellow fever and laria. It has had little effect, however, upon the generative diseases, and these are increasing as the mination of the infectious diseases lengthens the an of life.

Mills's thesis is that we fail to conquer the degenerave diseases because we do not recognize that their jor cause is the incessant drive of cool, stormy and riable climates, which reach their greatest extreme the north central United States. The most valuable rt of his book is a series of maps showing that the ath rate from a considerable series of diseases inases from south to north in the United States, and ries in corresponding fashion according to the clite of other parts of the world. The diseases include abetes, goiter, pernicious anemia, leukemia, pneunia, tuberculosis, appendicitis, arteriosclerosis and art failure. Suicides and homicides behave in much same way. Most of the diseases show a maximum ath rate in winter and a minimum in summer. Mills ows that in general the geographical distribution of ortality from these diseases is the same for whites d Negroes, and also for both rural and urban popuions. The Negro death rate, to be sure, always exeds that of the whites, and the urban and rural rates y differ. In all cases, however, the variations from gion to region are similar.

Mills takes issue with Winslow, Herrington and hers who claim that such diseases owe their disbution mainly to urban conditions and to the insity of modern industrial life. To the reviewer it ems that Mills does not pay enough attention to the t that even in villages our modern urban and instrial life is quite highly developed, and that it rely has an effect upon health in general and upon tabolism in particular. On the other hand, Winsw and his coadjutors fail to pay enough attention the fact that this kind of life is found only in clites that are highly stimulating, and that it would t be there to any such degree if the climate were fferent.

Another important point made by Mills is that in ny infectious diseases the number of *cases* is espelly high in the more stimulating climates, but the *aths* in proportion to the cases are few. In warmer imates, on the contrary, the number of cases is small, but the death rate in proportion to the cases is high. His interpretation of this is that although the overstimulation of the cool stormy type of climate leads to degeneration of certain organs, its general effect on the body is so good that people are often able to overcome disease. In warm monotonous climates, on the contrary, if people become ill for any cause whatsoever, they have relatively little power of resistance. There the number of deaths is high in proportion to the cases, although absolutely low. In this connection Mills finds that China and, to a less degree, Japan behave like tropical countries. Western Europe is more like the eastern United States, while the north central part of this country is peculiarly subject to the stimulus and the diseases induced by low temperature and great storminess.

Here is Mills's own way of putting his main conclusion: "Atmospheric turbulence, with sudden changes in temperature and barometric pressure, is a factor largely responsible for the initiation of infectious attacks, particularly in the respiratory and enteric systems. But ability to successfully resist the invasion seems to depend closely on the energy level engendered in the population mass by the stimulation of the climatic habitat. People living at low levels of energy and bodily vigor in regions of moist heat show little ability to throw off infections that once gain a foothold. Fortunately, in most tropical regions of moist heat, atmospheric stability is the rule. Only in the somewhat limited areas of tropical typhoons is man doubly handicapped in his struggle for survival. In these regions such infectious (?) diseases as tuberculosis, leprosy, acute nephritis and acute appendicitis take heavy toll. In the cooler portions of the stormy temperate regions ability to fight infectious invasions rises to much higher levels. There it is that most remarkable advances have been made in the fight to lessen the infectious disease death rates. But while these advances are being recorded, energetic inhabitants of these stimulating regions are exhibiting an increasing rate of exhaustion and bodily breakdown that provides an evil foreboding of what may eventually result from the too intensive climatic drive (pp. 161–2)."

In spite of much that is convincing, "Medical Climatology" needs greater precision. For example, "in Greenland the Norse colonies died out around 1000 A.D. (page 278)." That is the time when they went there. They disappeared four centuries later. Again page 256 mentions "a time when Pittsburgh has just become adapted to heat more severe than that of Texas." The reader understands that Pittsburgh, where the average July temperature is 75°, has a hotter season than Texas, where the July average at altitudes under 3,500 feet is 80° to 88°. Mills fails to explain that he refers to a particular instance when a brief heat wave made Pittsburgh hotter than Texas.

Much more important is the author's uncertain attitude toward changes in barometric pressure, an attitude which is prevalent among many others. For instance, "Tropical typhoon storms sweeping eastward over the West Indies and Caribbean region bring added instability during the winter months. These latter storms cause little temperature change, but their sharp pressure fluctuations seem to bring many of the same body disturbances that are associated with temperate zone storm changes [page 222]. . . . There is a strong suggestion that the sudden change of barometric pressure which accompanies tropical hurricanes may be just as important a factor in promoting many types of infectious diseases as are similar changes accompanying temperate zone storms [page 216]. Nevertheless, ". . . our knowledge of the physiologic effects induced by pressure changes is still far too incomplete even to be called evidence. There are hints, however, that fluctuations in atmospheric pressure do result in marked alterations in certain body functions, particularly those of the nervous system, reflex acts and glandular activity [page 258]. . . . The only significant experimental results so far published," however, "are those of Smith, showing a positive water balance in the body with pressure reduction and a negative balance with pressure increase. Body tissues in this respect act as a sponge [page 54]." In spite of the scarcity of evidence, ". . . Sudden changes in air temperature and barometric pressure, as major storm disturbances sweep across the continent, seem to be the most potent factors predisposing to acute infectious attacks [page 123]."

In many other places changes in atmospheric pressure from day to day are mentioned as if on a par with changes in temperature. Smith's conclusions, to which Mills refers, are based on differences less than the probable observational error in one of his two experiments, and only a little larger in the other. Most writers on this subject take no account of the fact that whenever we drive among hills which cause our altitude to vary as much as three or four hundred feet, we subject ourselves to changes of pressure like those in an ordinary storm, but much more sudden. Nevertheless, no one is conscious of any effect. Mills tells us, however, that "tropical populations living in typhoon regions exhibit the world's most severe tuberculosis problems, . . . particularly . . . in such typhoon-afflicted regions as the Philippines . . . the West Indies, and parts of Mexico . . . that are battered by this type of storm disturbance [page 138]." The obvious implication of this last statement and of those previously quoted is that the changes in pressure accompanying typhoons or hurricanes, especially in winter, are a main cause of tuberculosis. This ascribes far too much to these tropical disturbances. In the West Indies as a whole, for example, there are on about four hurricanes per year on an average. In a one region there are far less. Jamaica, for examp near the center of the hurricane belt, had only 14 36 years. Moreover, there are few hurricanes in wint as appears from the following data as to their to number in the entire West Indies from 1876 to 191

Jan.	0	Apr.	0	July	5	Oct.	
Feb.	0	May	1	Aug.	35	Nov.	
Mar.	0	June	8	Sept.	45	Dec.	

Another feature of "Medical Climatology" whi will at least arouse discussion is the map of climat stimulation on page 82. It is based on (1) the diff ence between the maximum and minimum temperatu of each day, (2) the difference between the maxima successive days, (3) the difference between the mini of successive days, and (4) the number of days havi temperatures above 64° and below 38°. From t standpoint of ordinary climatology and geography t resultant map seems inconclusive. It brings togeth regions which have little unity from the standpoin of vegetation, health or human activity. The greate climatic stimulation is indicated in places as diver as (1) the high Andean plateau within the tropics, (the plateau of Tibet, 25° farther north, (3) the plai of North America from Nebraska to the Arctic Circ and (4) New Zealand. The northeastern Unit States, the North Sea region of Europe and a va area in central Siberia, although reckoned by Mills highly stimulating, are placed in a lower categor It must be clearly understood, however, that Mills di tinguishes sharply between climatic stimulation a climatic efficiency. His whole book centers around t idea that the climate of some regions is so stimulati that its beneficial effect is in part counteracted.

In spite of these criticisms Mills's book is of hi value. It blazes a pioneer trail in its suggestion th the study of climate may be the clue which will le ultimately to a reduction in metabolic or degenerati diseases comparable to that which has taken place infectious diseases. It also contains a number of inte esting minor suggestions. For example, the place f sanitaria is not where a given disease is most commo but where it is rarest because that is where the clima helps to eliminate the disease. If all lepers were tak to Switzerland, the disease would presumably disa pear. Again, dental caries increases not only fro south to north in the United States, but as one go downward in river valleys. In a book where so man new ideas are set forth, the chance for error is nece sarily great. On the other hand, the searcher f fruitful research problems in the rich new field of t influence of physical environment will find in this boo a perfect mine of valuable suggestions.

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SPECIAL ARTICLES

THE BACTERIOSTATIC ACTION OF SULFANILAMIDE UNDER ANAEROBIC CONDITIONS

ALTHOUGH the therapeutic use of sulfanilamide and ied compounds has been attended with much clinical ccess, the mechanism of their action in overcoming rious infections is still in dispute. The *in vitro* udies of Locke,[1] Fox and coworkers[2] and the theoreti- deductions of Shaffer[3] have led many investigators assume that sulfanilamide is bacteriostatic only in presence of oxygen. Contrary to such claims are important findings of Bliss and Long[4] who re- rted bacteriostasis of streptococci and pneumococci der anaerobic conditions. However, Fox[5] claimed at Bliss and Long had been unable to obtain complete aerobiosis in their experiments and attributed these sults to small amounts of oxygen still remaining in ir media.

We wish to report some data which completely sub- ntiate the claim of Bliss and Long that sulfanil- ide may be bacteriostatic under anaerobic condi- ns. During the course of some experiments designed test the validity of the reduction potential theory of affer and of the anti-catalase hypothesis of Locke, have had occasion to examine the effects of lfanilamide on the growth of *E. coli*. This was done imarily because the respiratory mechanisms and nu- tional requirements of this organism are better derstood than are those of the coccus group and cause it has been pointed out[6] that *E. coli* is an cellent test organism for the accumulation of hydro- n peroxide.

Sulfanilamide produces, under given circumstances, rked bacteriostasis in cultures of *E. coli*. Thus, in dinary meat extract broth, bacteriostasis is observed der aerobic but not under anaerobic conditions. On other hand, in broth containing 1 per cent. glucose, lfanilamide produces but little effect. It might be imed that this protective action of glucose is attrib- able to its powerful reducing properties. Such does t appear to be the case, however. Both cysteine and corbic acid, powerful reducing agents themselves, il to protect against the sulfanilamide bacteriostasis. rthermore, as will be reported in another paper, glucose does not protect against the activity of sulfanilamide towards *E. coli* in certain other media.

It appears more probable that the protective action of glucose is based on its ability to supply to the cell a source of food and energy that is unaffected by the presence of sulfanilamide. *E. coli*, when growing in nutrient broth, depends on the various constituents of this medium for its supply of food materials, and if sulfanilamide, for any reason whatsoever, prevents the assimilation of various of these the growth of the cells will be adversely affected. On the other hand, if another substance (glucose) assimilable in nutrient broth even in the presence of sulfanilamide is added to the basal medium, growth will not be affected to any noticeable degree provided that such a substance can supply energy sufficient to permit growth to the same degree as do the constituents of the basal medium.

The proposition that sulfanilamide inhibits the mechanisms which enable the organism to grow aerobically at the expense of the constituents of nutrient broth finds some support in the following facts (Table I). *E. coli* grows well aerobically in nutrient broth

TABLE I

THE EFFECT OF SULFANILAMIDE ON GROWTH OF *E. coli* IN NUTRIENT BROTHS

Oxygen tension	Nutrient broth enriched with 1 per cent. glucose			
	Sulfanilamide 10 mg per cent.	———	Sulfanilamide 10 mg per cent.	———
Aerobic	++++	++++	+	+++
Anaerobic	++++	++++	+	+

but only poorly under anaerobic conditions. In the presence of oxygen, the energy required for the multiplication of such a facultative anaerobe as *E. coli* is obtained simultaneously from two different sources—the one, an aerobic, the other an anaerobic mechanism. If sulfanilamide inhibits only the aerobic mechanism, the degree of growth in the presence of this chemical and oxygen should approximate that obtained in the absence of oxygen, and sulfanilamide should have no effect under conditions which induce anaerobiosis. Such is actually the case.

Moreover, since the addition of glucose enables the organisms to grow luxuriantly both in the presence and absence of oxygen, neither type of growth in glucose broths should be affected by sulfanilamide if the latter does not inhibit the assimilation of glucose. The results in Table I demonstrate that both aerobic and anaerobic growth in glucose broth are the same in the presence as in the absence of sulfanilamide.

[1] A. Locke, E. R. Main and R. R. Mellon, SCIENCE, 88: 0, 1938.
[2] C. L. Fox, B. German and C. A. Janeway, *Proc. Soc. p. Biol. Med.*, 40: 184, 1939.
[3] P. A. Shaffer, SCIENCE, 89: 547, 1939.
[4] E. Bliss and P. Long, *Proc. Third Internat. Microbiol. ng.*, New York, 1939.
[5] C. L. Fox, *Proc. Third Internat. Microbiol. Cong.*, w York, 1939.
[6] R. H. Broh-Kahn and I. A. Mirsky, *Jour. Bact.*, 35: 5, 1938.

The type of bacteriostasis that has just been described is quite similar to that observed in the case of the hemolytic streptococci, since there is in both cases the same lag period before the bacteriostatic action becomes evident.

Quite different results were observed when the organism was grown in a synthetic medium of the following composition:

4.0 g. $(NH_4)_2HPO_4$	0.7 g. $MgSO_4$
1.0 g. NaCl	Trace $FeSO_4$
1.0 g. KH_2PO_4	1000 cc. distilled water

Adjust to pH 7

As has been demonstrated by Quastel *et al.*,[7] *E. coli* grows well aerobically in such a medium when 1 per cent. lactate is added, but not at all under anaerobic conditions. On the other hand, the addition of both 1 per cent. lactate and 1 per cent. nitrate enables the organisms to grow anaerobically as well as aerobically, since the cells can utilize the energy obtained from the oxidation of lactate by nitrate to multiply in the absence of oxygen.

When sulfanilamide is added to cultures growing aerobically in the lactate medium, very little bacteriostasis is evident. The same is true for aerobic cultures growing in the lactate-nitrate medium. However, anaerobic cultures in the latter medium are markedly inhibited by the action of sulfanilamide. This, then, is an example of a case in which sulfanilamide is bacteriostatic in anaerobic but not in aerobic environment.

It is apparent that sulfanilamide prevents the oxidation of lactate by nitrate and so exerts its effect in anaerobic cultures. In this respect its action is similar to that of the cyanides (Table II).

THE EFFECT OF SULFANILAMIDE AND CYANIDES ON THE GROWTH OF *E. coli* IN A SYNTHETIC MEDIUM

Oxygen tension	Synthetic medium + 1 per cent. Lactate enriched with					
			———	1 per cent. nitrate		
	Sulfanilamide 10 mg per cent.	KCN M/400	——	Sulfanilamide 10 mg per cent.	KCN M/400	——
Aerobic ..	++	++	++	+++	++	+++
Anaerobic .	—	—	—	—	—	+++

These results are not affected by the various methods employed to obtain anaerobiosis, and they have been observed under conditions in which the oxygen content is so low that it will not affect electrode potentials or reoxidize leuco dyes. The following biological criteria of anaerobiosis could be obtained under the conditions employed. It is known[8] that *E. coli* is extremely sensitive to oxygen when grown in media containing cyanides and certain reversible oxidation-reduction systems. Furthermore, the growth of *H. influenzae* in the absence of hemin is inhibited by the slightest traces of oxygen in the medium[9] and our methods of securing anaerobiosis were sufficient to permit the growth of both organisms under the conditions mentioned. Certainly, the few molecules of oxygen that remain in the medium are insufficient to produce enough peroxide, "blue substance"[10] or oxidized sulfanilamide to cause bacteriostasis.

These observations of the differences between the effects of sulfanilamide in the nutrient broths and in synthetic media suggest that sulfanilamide selectively inhibits only certain mechanism. It follows that if, perchance, such mechanisms are either essential or beneficial to multiplication, the growth of the organism will be inhibited to a greater or less extent.

The above results should not necessarily be construed to indicate that the theories of Locke, Shaffer and Fox may not explain the bacteriostasis observed *in vitro* under special conditions, but they appear to demonstrate that such mechanisms can not be the sole ones concerned. Experiments in this laboratory have led us to believe that the bacteriostasis produced by sulfanilamide and allied compounds can not be attributed to any general, non-specific mechanism and that all efforts to derive knowledge concerning its mode of action will be futile unless its effects are examined in a variety of media under different conditions.

This work has been carried on with the technical assistance of Dan Perry.

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EFFECT OF NICOTINAMIDE ON RESPIRATION OF DYSENTERY BACILLI

NICOTINIC acid has been shown to be essential for the growth of the dysentery organism on a synthetic medium composed of amino acids, glucose and salts.[1] Derivatives of nicotinic acid such as the amide, coenzyme I and coenzyme II, and other closely related compounds will also function as growth factors in a synthetic medium.[2] On the other hand, Lwoff and Lwoff have shown[3] that *Hemophilus parainfluenzae*

[7] J. H. Quastel, M. Stephenson and M. Whetham, *Biochem. Jour.*, 19: 304, 1925.

[8] R. H. Broh-Kahn and I. A. Mirsky, *op. cit.*

[9] T. L. Snyder and R. H. Broh-Kahn, *Nature*, 142: 153, 1938.

[10] C. L. Fox, B. German and C. A. Janeway, *op. cit.*

[1] Koser, Dorfman and Saunders, *Proc. Soc. Exp. Biol. Med.*, 38: 311–13, 1938.

[2] Dorfman, Koser, Reames, Swingle and Saunders, *Jour. Infectious Diseases*, 65: 163–82, 1939.

[3] *Proc. Roy. Soc., London*, B122: 352–9, 1937.

needs the entire molecule of coenzyme I or coenzyme II and can not synthesize it from nicotinamide. The dysentery organism when grown on a synthetic medium with nicotinamide can synthesize a compound (or compounds) identical with or an adequate substitute for one or more of the coenzymes needed by *H. influenzae*.[2]

By means of the Thünberg technique, Lwoff and Lwoff have shown[4] that *H. parainfluenzae* cells grown in a medium which is deficient in the "V" factor (presumably coenzyme I or coenzyme II) have their respiration markedly stimulated by the addition of coenzyme I or coenzyme II to the Thünberg tubes. A similar stimulation of oxygen uptake could be demonstrated by means of the Warburg technique. This stimulation disappears when the cells are grown in a medium containing larger amounts of "V" factor, *i.e.*, the addition of coenzymes to the Thünberg tubes does not increase the respiration.

We have performed similar experiments in which we used dysentery bacilli grown on a medium containing suboptimum amounts of nicotinamide. We found that the rate of reduction of methylene blue is greatly increased not only by the addition of coenzyme I, but also by the addition of nicotinamide or nicotinic acid to the Thünberg tube, as shown by the following protocol. This effect of nicotinamide and nicotinic acid has not previously been reported for any system. The cells (Strain D76) were grown 24 hours in synthetic medium containing 0.005γ nicotinamide. The cells from 100 cc of medium were collected in the centrifuge and suspended in M/20 buffer (pH 7.4). The cells were again centrifuged and suspended in 34 cc of buffer. Two cc of this suspension was added to each tube. Each tube also contained 0.30 cc of a 2 per cent. solution of glucose and 0.50 cc of a solution of methylene blue containing 100γ of methylene blue per cc. The nicotinamide and nicotinic acid solutions contained 100γ per cc. The cozymase solution contained 300γ per cc and was 40 per cent. pure. Smaller quantities of a pure cozymase preparation from Euler's laboratory showed the same effect. Water was added to the controls to make the dilution the same in all cases. The tubes were equilibrated 10 minutes at 37° before tipping.

TABLE 1

Tube	Control	1	2	3
Nicotinamide	0	0.15 cc	0	0
Nicotinic acid	0	0	0.15 cc	0
Cozymase	0	0	0	0.15 cc
Time (in sec.)	460	170	170	200

If we consider the ratio of the time of reduction control/nicotinamide, we find that the ratio decreases as the amount of nicotinamide in the *medium* is increased until with cells grown in a medium containing 0.020γ per cc it is about one. Thus at 0.003γ, the ratio is 3.8; at 0.005γ, 2.6; at 0.007γ, 1.8; at 0.010γ, 1.5; and at 0.020γ, 1.1. In controls containing nicotinamide, etc., but not glucose, reduction was much slower, 600 seconds or more. In controls which contained cells alone the methylene blue was reduced even more slowly or not at all. Nicotinamide, nicotinic acid or cozymase and glucose gave no reduction of methylene blue in the absence of cells.

The same stimulation of respiration by nicotinamide, etc., was found when oxygen uptake was measured by the direct Warburg method. It should be emphasized that various strains of the dysentery organism differ in their nicotinamide requirements. Further work in an attempt to elucidate the mechanism of this codehydrogenase action of nicotinamide is in progress in this laboratory.

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SOMATOPLASTIC STERILITY IN MEDICAGO SATIVA[1]

THE collapse of ovules during the early stages of post-fertilization development frequently occurs in alfalfa, particularly after self-pollination.[2] Histological study shows that the collapse follows abnormal growth of the somatic tissue adjacent to the embryo sac. Since local hyperplasia of the maternal structures appears to be the essential feature of the developmental course leading to collapse, the term somatoplastic sterility is here proposed for a type of seed failure believed to occur in many plants.

The reproductive process in angiosperms may fail at any stage between fertilization and maturity of the seed. The early stages are of critical importance for survival of the ovule in alfalfa. Although somatoplastic sterility is not necessarily limited to this period, it is in young ovules that one would expect it to be manifested in simplest form. The case is of interest, therefore, as affording a point of departure in defining the significant histological features and in discovering the cause of a rather obscure, although probably widespread, form of sterility in plants.

The embryo sac in the mature ovule of alfalfa is surrounded by two integuments. The inner integument, which is composed of two layers of cells, lies in direct contact with the embryo sac except at the chalazal end where a few disintegrating cells, remnants of

[4] *Ibid.*, 360–73.

[1] Papers from the Department of Genetics, Agricultural Experiment Station, University of Wisconsin No. 248. The authors desire to express their appreciation for financial aid from the University Research Committee and for assistance from WPA project in the Natural Sciences No. 8649.

[2] Brink and Cooper, *Proc. Nat. Acad. Sci.*, 24: 497–499, 1938.

the nucellus, are found. Shortly after fertilization active cell division is initiated in the integuments as well as in the endosperm mother cell and the zygote. The cells of the inner integument divide longitudinally so that this tissue normally continues to have two layers of cells at the later stages of development. The cells adjacent to the endosperm are tapetal-like in appearance.

In material collected 48 to 72 hours after pollination in which the collapse of fertile ovules is frequent the cytoplasm of the cells immediately adjacent to the endosperm becomes finely vacuolate and densely staining, and the resemblance to tapetal cells is gradually lost. This condition, which makes its first appearance on the funicular side of the ovule in the region of the vascular bundle, is often seen before any impairment of the embryo sac becomes evident. Breakdown of the endosperm follows, beginning in the chalazal region and progressing toward the embryo. At this stage there is extensive meristematic activity in the chalazal portion of the inner integument. Through transverse division of the cells this tissue may come to be three to five layers in thickness. The ovule may continue to enlarge for several hours, even after the endosperm has broken down, but its growth soon ceases.

The frequency of collapse of fertile ovules in alfalfa is much higher following self-pollination than after outcrossing to unrelated plants. In a representative experiment involving seven individuals on which the two types of matings were made under strictly comparable conditions the average values were 34.4 per cent. and 7.1 per cent., respectively, in the interval up to 144 hours after pollination.[2] The relatively high survival of ovules containing hybrid, as compared with inbred, embryos and endosperms affords a clue to the cause of somatoplastic sterility.

Fertilization initiates development of the embryo and the endosperm and stimulates mitosis in the surrounding somatic tissue. The ovule, quiescent prior to gametic union, suddenly springs into active growth. Further development of these structures is largely dependent upon food moved in from other parts of the plant, the visible reserves immediately at hand in alfalfa being very limited in amount and quickly disappearing after fertilization. The critical factor for survival at this stage seems to be the manner in which the translocated food is shared between the endosperm, on the one hand, and the inner integument, on the other. The partition of nutrients appears to depend upon the rate of growth inside and outside the embryo sac. It may be assumed that the synthetic processes are essentially alike in the different tissues concerned, and hence, that the same raw materials are in concurrent demand. Under these conditions of parallel growth the available foods will be shared between the inner integument and the structures within the embryo sac in proportion to the velocity with which growth is occurring in the respective tissues. Continued development of the ovule following fertilization demands a balance in rate of growth between the endosperm, which is the dominant tissue within the embryo sac, and the adjacent maternal tissue which will insure the nourishment of both. If, during early development, the balance is upset by failure of the endosperm to keep pace with growth in the extensive surrounding tissue the endosperm starves and, eventually, the ovule collapses.

Following hybridization in alfalfa, the rate of growth of the endosperm, as measured by the number of nuclei, is found to be significantly higher than after selfing. The two classes of embryos, on the other hand, grow at only slightly different, and much lower, rates. As mentioned above, only about one fifth as many fertile ovules collapse after crossbreeding as after selfing. The initial conditions in the ovule outside the embryo sac being alike in the two cases, it seems clear that the higher survival following crossing is the result of the more active growth of the hybrid endosperm. Conversely, following self-fertilization, the rate of growth of the endosperm is frequently so low that the balance soon shifts in favor of the integument. The hyperplasia we have described then arises, causing collapse of the endosperm and, eventually, terminating development of the ovule.

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